VOLUME 61 NUMBER 1

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JANUARY 1950

PUBLISHED MONTHLY BY AMERICAN MEDICAL ASSOCIATION, 535 NORTH DEARBORN STREET, CHICAGO 10, ILLINOIS. ANNUAL SUBSCRIPTION, $12.00

Entered as Second Class Matter Oct. 30, 1917, at the Postoffice at Chicago, Under the Act of Congress of March 3, 1879

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Archives of Dermatology and Syphilology

VOLUME 61 JANUARY 1950 NUMBER 1

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CUTANEOUS CHANGES IN LUPUS ERYTHEMATOSUS

Histopathologic Aspects, with Special Reference to Vascular Changes

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AND
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A REVIEW of lupus erythematosus has been presented in numerous papers.[1] The present paper deals with the cutaneous histopathologic aspects of lupus erythematosus, with special reference to the vascular changes within the cutis. It will include a review of the literature directly pertaining to the subject.

REVIEW OF THE LITERATURE

Although the histopathologic changes within the epidermis are secondary to changes within the cutis, they are nevertheless considered to be of great diagnostic significance.[2] The changes within the epidermis

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Abridgment of thesis submitted by Dr. McCreight in August 1948 to the Faculty of the Graduate School of the University of Minnesota in partial fulfilment of the requirements for the degree of Master of Science in Dermatology and Syphilology.

1. (*a*) Kaposi, M.: Neue Beiträge zur Kenntniss des Lupus erythematosus, Arch. f. Dermat. u. Syph. **4**:36, 1872. (*b*) Klemperer, P.; Pollack, A. D., and Baehr, G.: Pathology of Disseminated Lupus Erythematosus, Arch. Path. **32**:569 (Oct.) 1941. (*c*) Madden, J. F.: Acute Disseminated Lupus Erythematosus, Arch. Dermat. & Syph. **25**:854 (May) 1932. (*d*) Michelson, H. E.: The Problem of Lupus Erythematosus, California Med. **70**:5 (Jan.) 1949. (*e*) Montgomery, H.: Disseminate Lupus Erythematosus as a Systemic Disease, in Christian, H. A.: The Oxford Medicine, New York, Oxford University Press, 1939, vol. 4, pt. 1, chap. 1-C, pp. 44(41)-44(65). (*f*) Montgomery, H., and McCreight, W. G.: Disseminate Lupus Erythematosus, Arch. Dermat. & Syph. **60**:356 (Sept.) 1949. (*g*) Ormsby, O. S., and Montgomery, H.: Diseases of the Skin, ed. 7, Philadelphia, Lea & Febiger, 1948, pp. 944-963. (*h*) O'Leary, P. A.: Disseminated Lupus Erythematosus, Minnesota Med. **17**:637 (Nov.) 1934.

2. (*a*) Gans, O.: Histologie der Hautkrankheiten: Die Gewebsveränderungen in der kranken Haut unter Berücksichtigung ihrer Entstehung und ihres Ablaufs, Berlin, Julius Springer, 1925, vol. 1, pp. 534-547. (*b*) Goeckerman, W.

(Footnote continued on next page)

consist in hyperkeratosis without parakeratosis, keratotic plugging of the hair follicles and glandular orifices and, independent of the foregoing, atrophy and adjacent acanthosis of the rete mucosa and liquefaction degeneration of the basal cell layer.

The histopathologic changes within the cutis are variable; so far as subacute disseminated lupus erythematosus and acute disseminated lupus erythematosus are concerned, there are divergent opinions regarding the interpretation of these changes.

Edema within the cutis is a reversible reaction and may be either intracellular or intercellular. It is most pronounced in the area of the papillary bodies.

Klemperer, Pollack and Baehr [1b] reported hyalinization and fibrinoid degeneration of the connective tissue within the cutis but stated that it is less conspicuous than degeneration and necrosis of fibroblasts. Unna [2e] and Fordyce and Holder [3] called attention to hyalinization of connective tissue within the papillary bodies.

The elastic tissue of the cutis may be unaltered in early lesions of lupus erythematosus; however, in older lesions in which there is a well marked cellular infiltrate the elastic tissue may be entirely destroyed in the areas of infiltration.

Satenstein [4] wrote that merging of elastic and connective tissue fibers within the cutis was necessary for the histologic diagnosis of lupus erythematosus. However, Goeckerman and one of us (H. M.) [2b] found that this change is present in other conditions, may occur at any age and is present only in specimens removed from exposed surfaces of the body.

The earliest changes to occur within the cutis are those of dilatation of the superficial capillaries and lymphatic vessels, together with edema of the walls of these vessels and the extravasation of leukocytes and, after a time, lymphocytes and monocytes. Later in the course of

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H., and Montgomery, H.: Lupus Erythematosus: An Evaluation of Histopathologic Examinations, Arch. Dermat. & Syph. **25**:304 (Feb.) 1932. (*c*) Kaposi, M.: Pathology and Treatment of Diseases of the Skin for Practitioners and Students, translated by J. C. Johnston, New York, William Wood & Company, 1895, pp. 505-510. (*d*) Montgomery, H.: Pathology of Lupus Erythematosus, J. Invest. Dermat. **2**:343 (Dec.) 1939. (*e*) Unna, P. G.: The Histopathology of the Diseases of the Skin, translated by N. Walker, New York, Macmillan & Co., 1896, pp. 1071-1081.

3. Fordyce, J. A., and Holder, O. H.: Some Clinical Observations of Lupus Erythematosus: The Pathology of Lupus Erythematosus, M. Rec. **58**:41 (July 14) 1900.

4. Satenstein, D. L., in discussion on Goeckerman and Montgomery,[2b] p. 314.

development of the lesions, a variable number of pigment-laden chromatophores may be found in the infiltrate. Baehr, Klemperer and Schifrin [5] were able to view the dilated capillaries in involved skin about the nail bed by use of a capillary microscope. Klemperer, Pollack and Baehr [1b] described the extravasation of erythrocytes through the wall of dilated capillaries, even though the capillary endothelium remained unaltered.

Occlusion of the lumens of blood vessels of the skin was reported by Leloir [6] and Fordyce and Holder.[3] Gans [2a] stated that this was a rare observation. Keil [7] reported partial occlusion of the lumens of blood vessels produced by mural thrombi and hyaline thrombi. Baehr, Klemperer and Schifrin [5] found proliferative lesions of the lining endothelium of capillaries, arterioles and venules associated with obstruction of the lumen by thrombi. One of us (Montgomery) found true proliferative and obliterating changes in vessels of the skin only in lesions which had been exposed to local radiotherapy. Goeckerman and one of us (H. M.) [2b] found partial or complete occlusion of some superficial vessels as the result of edema of walls of individual vessels.

In the larger vessels, arterioles and arteries of the skin, Klemperer, Pollack and Baehr [1b] found the same degenerative phenomena as in vessels of other organs of patients with lupus erythematosus. They reported the presence of homogeneous eosinophilic material (fibrinoid) within the intima, between the muscle fibers of the media and within the adventitia, usually accompanied with proliferation of fibroblasts.

Changes in the blood vessels in other organs of the body were reported by a number of authors, and the literature was reviewed in recent publication.[8]

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5. Baehr, G.; Klemperer, P., and Schifrin, A.: A Diffuse Disease of the Peripheral Circulation (Usually Associated with Lupus Erythematosus and Endocarditis), Tr. A. Am. Physicians **50**:139, 1935.

6. Leloir, H.: Recherches sur l'histologie et pathologie et la nature du lupus érythémateux, Arch. de physiol. norm. et path. **2**:690, 1890.

7. Keil, H.: Conception of Lupus Erythematosus and Its Morphologic Variants, with Particular Reference to "Systemic" Lupus Erythematosus, Arch. Dermat. & Syph. **36**:729 (Oct.) 1937.

8. Klemperer, Pollack and Baehr.[1b] Ormsby and Montgomery.[1g] Baehr, Klemperer and Schifrin.[5] Daly, D.: Central Nervous System in Acute Disseminate Lupus Erythematosus, J. Nerv. & Ment. Dis. **102**:461 (Nov.) 1945. Humphreys, E. M.: The Cardiac Lesions of Acute Disseminated Lupus Erythematosus, Ann. Int. Med. **28**:12 (Jan.) 1948. Klemperer, P.: The Pathogenesis of Lupus Erythematosus and Allied Conditions, ibid. **28**:1 (Jan.) 1948. Rakov, H. L., and Taylor, J. S.: Acute Disseminated Lupus Erythematosus Without Cutaneous Manifestations and with Heretofore Undescribed Pulmonary Lesions, Arch. Int. Med. **70**:88 (July) 1942.

DERMATOHISTOPATHOLOGIC OBSERVATIONS

This study is based on the histologic review of 119 specimens removed for biopsy or postmortem examination from cutaneous lesions of lupus erythematosus. Eighteen specimens were removed from 16 persons with acute disseminated lupus erythematosus, 61 specimens from 42 persons with subacute lupus erythematosus, 23 specimens from 21 persons with chronic disseminated lupus erythematosus and 17 specimens from 17 selected persons with chronic discoid lupus erythematosus.

In the selection of specimens from the persons with chronic discoid lupus erythematosus, it was first determined that the individual lesions had not received any type of radiation therapy prior to removal of the the specimen and, second, that the specimen was considered histologically typical of lupus erythematosus.

All the specimens were fixed in either formaldehyde solution U. S.P. or 70 per cent alcohol. All specimens were routinely stained with hematoxylin and eosin and elastin H stains. For detection of possible changes in the connective tissue, van Gieson and Mallory-Heidenhain stains were used.

The same histologic changes within the epidermis found in the chronic discoid specimens also were found in the specimens from the disseminated types. However, the degree of change was less pronounced in the disseminated types.

Hyperkeratosis without parakeratosis was nearly a constant finding, as was also keratotic plugging, either follicular or extrafollicular. Atrophy and adjacent acanthosis of the rete mucosa, together with liquefaction degeneration of the basal cell layer, occurred in more than 90 per cent of the specimens. This observation is in general agreement with the reports of most authorities (fig. 1).

Edema of pronounced or moderate degree in the upper portion of the cutis was frequently observed; however, pronounced edema of the entire cutis was not observed in any specimen. Evidence of vesicle formation at the junction of the cutis and epidermis was noted in 6 specimens of disseminated lupus erythematosus.

Changes in the connective tissue were relatively infrequent and nonspecific in type. Intracellular edema of connective tissue fibers to an appreciable degree occurred in only 1 specimen from a patient with chronic disseminated lupus erythematosus and in 2 specimens from 2 patients with subacute disseminated lupus erythematosus. Hyalinization of connective tissue fibers seemed to be more frequent in the severe types of the disease and was found in 5 specimens from the acute disseminated and in 5 from the subacute disseminated type but in only 1 each from the chronic disseminated and chronic discoid types of the disease.

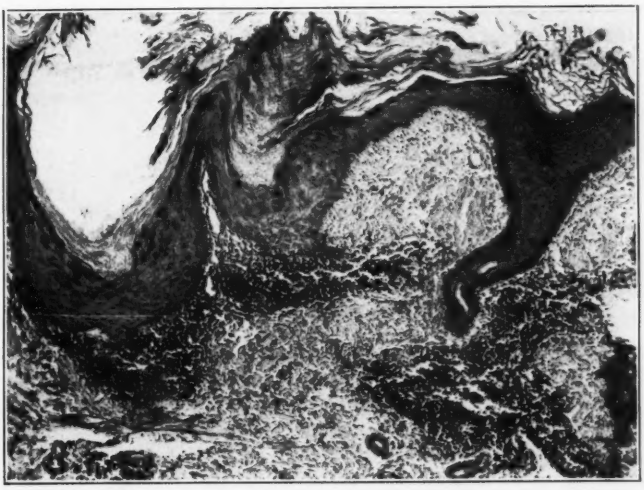

Fig. 1.—Chronic discoid lupus erythematosus, showing relative and absolute hyperkeratosis without parakeratosis, keratotic follicular and extrafollicular plugging, atrophy and adjacent acanthosis of the prickle cell layer, liquefaction degeneration of the basal cell layer and a lymphocytic cellular infiltrate distributed about the hair follicle and dermal appendages; hematoxylin and eosin stain, × 75.

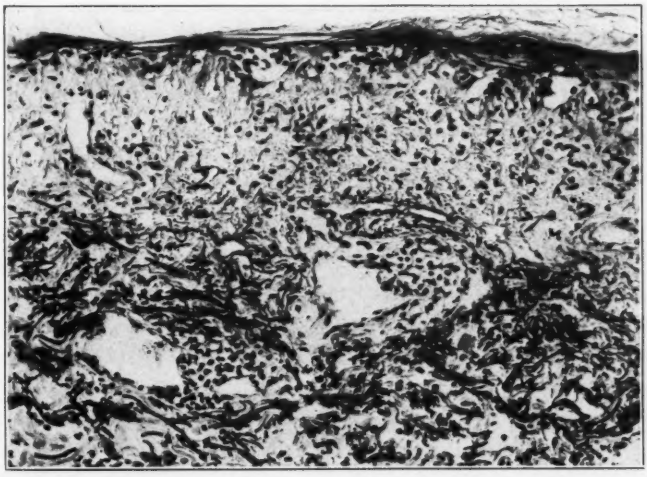

Fig. 2.—Subacute disseminated lupus erythematosus in specimen removed from neck, showing relative and absolute hyperkeratosis, extreme thinning of the prickle cell layer, liquefaction degeneration of basal cell layer and also dilatation of superficial capillaries and lymphatic vessels. Elastic fibers which stain black are frayed and splintered but not degenerated; elastin H stain, × 140.

Fibrinoid degeneration was noted in only 1 specimen from the acute disseminated type. However, fibroblastic proliferation was found in 2 specimens of the chronic discoid type.

Dilatation of the superficial capillaries alone or in combination with dilatation of the superficial lymphatic vessels was found in a total of 109 specimens. The walls of the capillaries were intact, in spite of the pronounced dilatation (fig. 2). Migration of erythrocytes through the capillary walls was found in 11 specimens, while migration of leukocytes through the capillary walls was noted in 5 specimens. Occasionally the capillary wall seemed to merge with the surrounding eosinophilic homogeneous connective tissue.

Three specimens from the chronic disseminated type, 3 specimens from the subacute disseminated type and 2 specimens from the acute disseminated type of the disease revealed evidence of endothelial proliferation occurring in the deeper vessels. There was no evidence of endothelial proliferation in the superficial vessels.

Evidence of degenerative phenomena within the walls of the vessels was relatively infrequent. In only 1 specimen from the chronic discoid type of lupus erythematosus was there degeneration to the point of almost complete obliteration of the lumen of an artery. Hyaline change within the walls of vessels was found in 1 specimen from a patient with chronic discoid lupus erythematosus, 5 specimens from the chronic disseminated type of disease, 4 from the subacute disseminated type and 5 from the acute disseminated type. Fibrinoid degeneration of the walls of vessels was found in 1 specimen from the chronic disseminated type, 2 from the subacute disseminated type and 1 from the acute disseminated type. The changes noted in these 4 specimens were so minimal that it was always a question whether they represented true fibrinoid degeneration or whether they were only secondary to edema and cellular reaction (fig. 3).

Edema of the walls of capillaries and the deeper vessels was noted in a total of 36 specimens. The edema was not limited to any one portion of the wall of a vessel but was distributed generally throughout the vessel. A hydropic appearance with small vacuolar areas was noted in some specimens.

A cellular infiltrate of variable amount occurring about the blood vessels or dermal appendages was found in nearly all the specimens. In 81 specimens this infiltrate consisted primarly of lymphocytes. Occasionally monocytes or leukocytes were noted. The infiltrate was generally found in the upper portion and the midportion of the cutis but seldom in the deep part of the cutis. The amount of cellular infiltrate seemed to have some relation to the severity of the disease and the duration of the individual lesion, being most pronounced in lesions of chronic discoid type and less evident in those of the acute disseminated type (fig. 4).

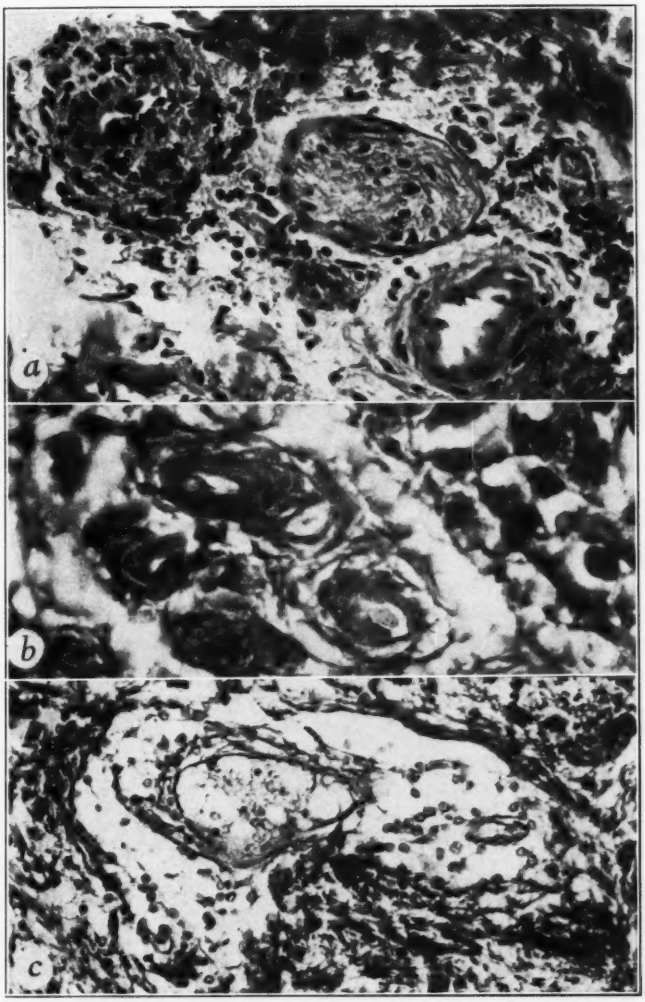

Fig. 3.—(*a*) Chronic discoid lupus erythematosus, showing partial occlusion of the lumen of an arteriole, endothelial proliferation and migration of leukocytes through the vessel wall; hematoxylin and eosin stain, × 300. (*b*) Acute disseminated lupus erythematosus, showing hyaline changes within the walls of vessels in the upper portion of the cutis; Mallory-Heidenhain stain, × 400. (*c*) Chronic disseminated lupus erythematosus, showing dilatation of a capillary and migration of erythrocytes through the intact wall of the capillary; Mallory-Heidenhain stain, × 300.

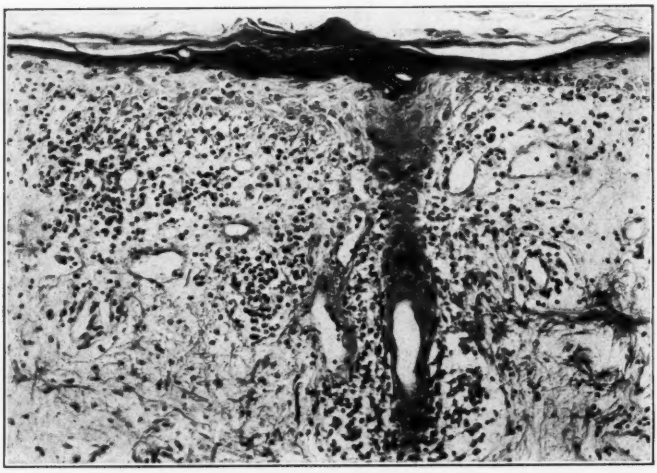

Fig. 4.—Acute disseminated lupus erythematosus, with histologic features of chronic discoid lupus erythematosus, illustrating that histologic differentiation of the various types of lupus erythematosus is difficult; hematoxylin and eosin stain, × 115.

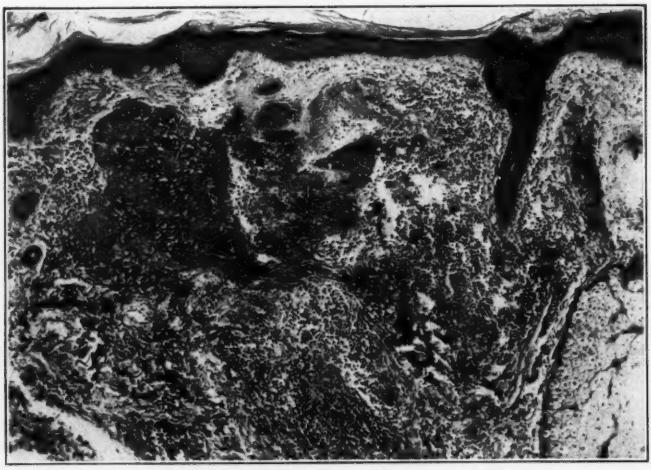

Fig. 5.—Chronic discoid lupus erythematosus in a specimen removed from a lesion on the face, illustrating the merging of elastic and connective tissue to form collacin; elastin H stain, × 55.

Senile changes (collacin) of the skin were noted in a total of 14 specimens; all these specimens had been removed from lesions occurring on the surfaces exposed to light (fig. 5).

Dilatation of the sweat glands, together with some atrophy of the epithelial cells of these glands, occasionally was noted. There was no noticeable evidence of hyperplasia or hypertrophy of the sebaceous glands.

Chromatophores laden with melanin pigment were seen in a total of 46 specimens, with the greatest frequency in specimens from the disseminated types of disease. These chromatophores occurred most often in the upper portion of the cutis, but occasionally they were distributed about the dermal appendages.

Fragmentation, splintering and edema of the elastic tissue were noted in 86 specimens. Complete destruction of the elastic tissue in areas of dense cellular infiltration was noted in only 7 specimens.

In addition to the specimens from lesions of lupus erythematosus, we studied 7 specimens from persons with clinical erythema multiforme in an attempt to determine whether changes in the vessels similar to those seen in lupus erythematosus might be present. In 5 of the 7 specimens there was the same evidence of dilatation of the superficial capillaries and lymphatic vessels. Five specimens revealed some thickening of the walls of the larger vessels; yet evidence of hyaline degeneration was not seen in any specimen. There was more of a tendency toward endothelial proliferation in this group than in the group of lesions of lupus erythematosus, and partial or complete occlusion of the lumens of vessels was more frequent. The infiltrate when present was almost always perivascular in distribution and was composed not only of lymphocytes but also, usually, of polymorphonuclear cells and sometimes eosinophils. There was no tendency for the infiltrate to be distributed about the dermal appendages. The changes in the epidermis were not at all like those of lupus erythematosus, since follicular plugging was not present and liquefaction degeneration of the basal cell layer was found in only 1 specimen of erythema multiforme. In the specimens from erythema multiforme there was a greater tendency toward the formation of vesicles and bullae. Atrophy and adjacent acanthosis of the prickle cell layer were noted in only 1 of the 7 specimens. In 3 specimens there was evidence of acidophilic staining of the epidermis.

COMMENT

It is apparent from the previous observations that there is no single pathologic change which will allow a definite diagnosis of lupus erythematosus. However, a combination of observations when considered together seems to be relatively specific. These are hyperkeratosis without

parakeratosis, keratotic plugging of hair follicles and glandular orifices or, independent of either, atrophy and adjacent acanthosis of the prickle cell layer, liquefaction degeneration of the basal cell layer, edema of the cutis, dilatation of the superficial capillaries and lymphatic vessels, a cellular infiltrate composed primarily of lymphocytes distributed about the vessels and dermal appendages, the presence of a varying number of chromatophores laden with melanin and the absence of obliterative or proliferative changes in walls of the deeper blood vessels.

The very infrequent finding of any evidence of hyaline changes within either the cutis or the vessels of the cutis would seem to be important, since this type of change has been reported much more frequently in other organs of the body. The cutis is such a rich bed of collagen tissue that it seems reasonable to expect more evidence of degenerative change if one is to accept the concept of lupus erythematosus as a disease of diffuse collagen degeneration. Since the vessels of the skin differ in no way from the vessels of other organs of the body, it might be expected that the same frequency of vascular change would be found within these vessels; yet it was not. Edema of the walls of vessels was the most frequent finding; yet this may be considered nonspecific in character. The only specimen which revealed evidence of occlusion of the lumen of an artery was from a lesion of chronic discoid lupus erythematosus.

It is impossible for one to distinguish the various types of lupus erythematosus histologically, since the microscopic appearance depends more on the age of the individual lesions than on the type of disease. An early lesion of chronic discoid lupus erythematosus may have the same histologic appearance as a well developed lesion from acute disseminated lupus erythematosus.

SUMMARY

The results of a histologic study of 119 specimens from cutaneous lesions of lupus erythematosus have been presented in this paper. One hundred and two of these specimens were from patients who had disseminated lupus erythematosus, and 17 specimens were from selected patients with chronic discoid lupus erythematosus. Special reference has been given to the vascular changes in these specimens.

The same histologic changes were noted in all the various types of lupus erythematosus. However, there was some variation in the degree of changes. This variation seemed to be dependent more on the age of the individual lesion than on the type of disease. Distinction of the type of the disease based entirely on the histologic picture is impossible.

Evidence of hyaline degeneration or fibrinoid degeneration within the collagen tissue of the cutis was relatively infrequent.

Edema of the walls of blood vessels was the most frequent vascular change noted. Although some evidence of hyaline degeneration within the walls of the vessels was noted, it was much less frequent than that which has been noted in the vessels of other organs of the body.

Occlusion of an artery due to degenerative changes was noted in only 1 specimen from the chronic discoid type of lupus erythematosus.

Senile changes of the skin were present only in specimens removed from lesions in areas of skin exposed to light.

LYMPHOSARCOMA TREATED WITH NITROGEN MUSTARD

Report of a Case

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H. A. CUMMING, M.D.

MINNEAPOLIS

AND

G. D. McAFEE, M.D.

CINCINNATI

THE USE of the nitrogen mustards in treatment of the lymphoblastoma group of diseases has recently aroused much interest among both clinicians and pathologists, but there are very few reports on the use of this drug in cases of lymphosarcoma cutis.

We had the opportunity to study, from the onset of the initial lesion until death twelve months later, a patient with lymphosarcoma cutis on whom nitrogen mustard therapy was used.

REPORT OF A CASE

A. R., a 75 year old white man, was first seen in the outpatient dermatology service at the Minneapolis General Hospital on Feb. 27, 1947. At that time his sole complaint was a dark red to purple plaque, located in the right preauricular region, which had been present for four weeks. A biopsy of this lesion showed microscopic changes consistent with a diagnosis of lymphorsarcoma. The patient was then admitted to the hospital for roentgen therapy, which he received between March 15 and April 24, 1947. After four weekly treatments of 100 r each, filtered through 1 mm. of aluminum, the lesion resolved quickly and completely, and the patient was discharged. He was followed in the outpatient clinic for an eight month period and on Jan. 18, 1948, he was persuaded to return to the hospital because of weakness, malaise, loss of weight and the development of many scattered new lesions similar in appearance to the original one.

The patient's past health had always been excellent, and he denied ever having been ill previously. He had never had any operations or suffered any serious injuries. His family history was noncontributory.

Physical Examination.—At the time of the patient's first admission on March 15, 1947, he was described as being a well developed, well nourished man who appeared to be younger than his age would indicate. Blood pressure at that time was reported as being 200 mm. of mercury systolic and 90 mm. of mercury diastolic. The heart was moderately enlarged, and there was a blowing systolic murmur heard best over the apex. There was a 2 plus pitting edema over the pretibial regions, ankles and feet. The only cutaneous lesion at this time was one elevated, firm, slightly tender, purplish plaque situated just anterior to the right ear. It measured 3 cm. by 4 cm.

From the Department of Dermatology and Syphilology, University of Minnesota, Dr. H. E. Michelson, director, and the Department of Dermatology and Syphilology, Minneapolis General Hospital, Dr. S. E. Sweitzer, chief.

Fig. 1.—Lymphosarcoma cutis, the eruption on the face being shown.

Fig. 2.—Lymphosarcoma cutis, with plaques and tumors on the thigh.

At the time of the patient's second hospitalization (Jan. 18, 1948) the physical examination had essentially the same results, with the exception of the observations on the skin. That of the head as well as of all other areas of the body was marked by scattered purplish red plaques of varying size. Some of them appeared as hemorrhagic, tender, indurated tumors of variable sizes, ranging from 1 to 10 cm. in diameter. The lesions were most numerous on the thighs, and only the hands and feet were free of any eruption.

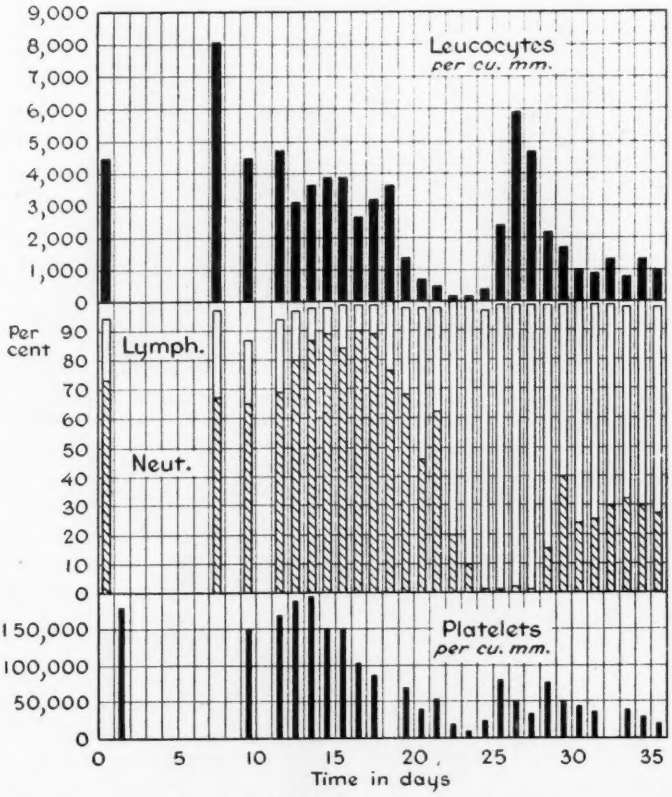

Fig. 3.—Graphic illustration of the white blood cell, differential and thrombocyte count.

Course.—At the time of the first hospitalization four roentgen radiation treatments of 100 r, each filtered with 1 mm. of aluminum, were given to the preauricular lesion on the right side of the face. This was the only lesion present and faded quickly. The tuberculin test, serologic studies of the blood, examination of the urine and studies by aspiration of bone marrow all had negative results. Studies of the blood showed moderate anemia with an erythrocyte count ranging between 3,800,000 and 3,200,000 cells per cubic centimeter. The thrombocyte count was

180,000 cells per cubic centimeter. The sedimentation rate was 66 mm. in one hour. Roentgen examination of the entire gastrointestinal tract showed normal conditions, as did the examination of the bones of both hands and feet. A roentgenogram of the chest taken at a distance of 6 feet showed slight cardiac enlargement of the left ventricular type, while the lungs were normal. The patient remained afebrile throughout the period of his first hospitalization.

During the eight months' interval between hospitalizations, the patient was treated with further roentgen radiation to new lesions which appeared over the left side of the face and to other parts of the body. It was noted that no new lesions developed in the area that had originally been irradiated, that is, the right preauricular region.

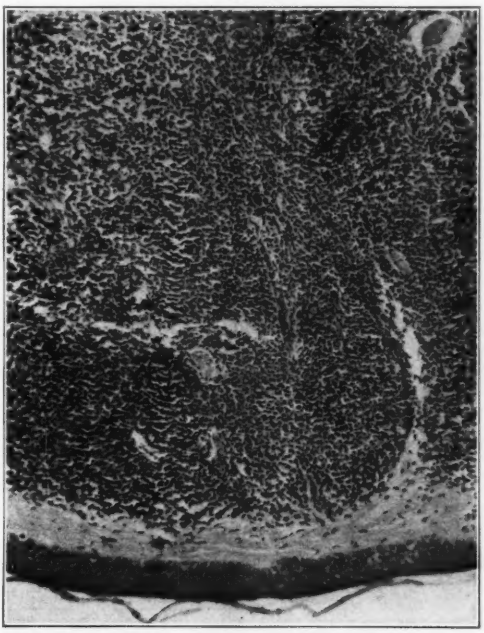

Fig. 4.—Lymphosarcomatous cells in the cutis.

With the rapid development of new lesions over widespread areas of the body, superficial roentgen therapy was no longer feasible. On Jan. 13, 1948, the patient was persuaded to reenter the hospital for the express purpose of receiving nitrogen mustard therapy.

Figure 3 illustrates the course of the patient's second hospitalization. The base line, calibrated in days, began on Jan. 14, 1948. The patient received 500 cc. of whole citrated blood on this day. On Jan. 21, 23, 25, and 27, 1948 (on days 8, 10, 12 and 14 in figure 3), he was given 6.8 mg. of methyl-bis (β-chloroethyl) amine hydrochloride plus 1,000 cc. of an isotonic solution of sodium chloride intravenously. The dosage recommended by Jacobson and Spurr was utilized, that is, an amount based on 0.1 mg. of nitrogen mustard per kilogram of body weight,

modified by administration of the drug on four alternate days rather than on four successive days. There were no gastrointestinal or other symptoms noted at the time of injection, and within a few days all lesions began to subside. The leukocyte count hovered around 4000 cells per cubic millimeter until Feb. 1, 1948, at which time there was a sudden drop in the total circulating white count. This began four days after the last intravenous injection of nitrogen mustard and reached its maximum five days later, on Feb. 6, 1948, at which time it was reported to be 150 cells per cubic millimeter. There was a sharp rise within a few days, but this was not sustained. The leukocyte level hovered around the 1,000 mark until the patient's death six days later.

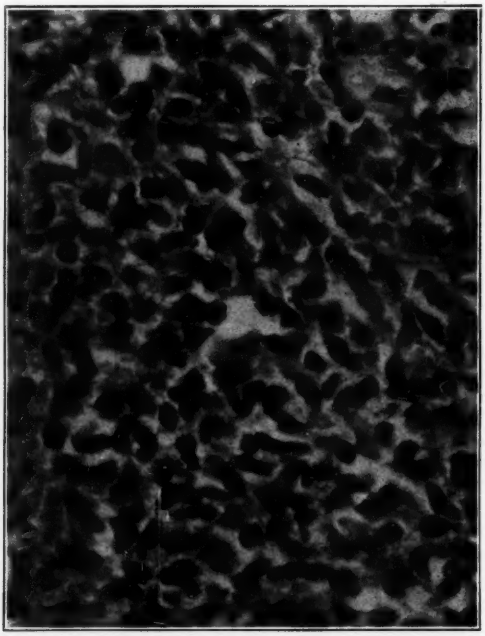

Fig. 5.—High power magnification of the lymphosarcomatous cells.

After the destruction of leukocytes, as observed by differential counts, it was seen that the neutrophils bore the brunt of the attack. During the most severe depression the neutrophils comprised only 1 to 2 per cent of the total white cell count.

The thrombocytes did not escape destruction, either. Their number dropped from 180,000 per cubic millimeter, reported on January 15, to a low of 10,000 on Feb. 13, 1948, nine days after the last injection of nitrogen mustard. At this time the patient experienced severe bouts of epistaxis and had hemorrhage into the resolving lymphosarcomatous cutaneous lesions and also into the gastrointestinal tract.

On February 3, the temperature rose to 104.6 degrees and remained elevated until the patient's death on Feb. 19, 1948. Because of the fever and the severe

agranulocytosis, 50,000 units of an aqueous solution of crystalline penicillin G was administered intramuscularly every three hours from February 3 until the patient's death, sixteen days later. In addition, nine more whole citrated blood transfusions of 500 cc. each were given on February 3, 4, 5, 6, 7, 8, 11, 13 and 17. Despite this supportive treatment and the gradual return of neutrophils to the circulation, the patient became steadily weaker and died from the prolonged effects of agranulocytosis directly due to the nitrogen mustard therapy.

The pathologist's report on the first biopsy, performed Feb. 27, 1947, gave the diagnosis as lymphosarcoma cutis. The biopsy specimen taken on March 31, 1947, showed a picture similar to that in the previous section except that the process appeared more advanced. The corium was deeply infiltrated by solid sheets of lymphoid cells, with reticulum hyperplasia also noted. Numerous mitotic figures were seen throughout all sections. Again a diagnosis of lymphosarcoma of the skin was made. Repeated biopsies, on January 21, and again on January 28, revealed the same pathologic features as had been previously reported. In most of the sections the subcutaneous tissues were infiltrated by sheets of pale-staining cells with large, pale nuclei. There was no tendency to form glands in any of the sections. Tissue imprints made from these biopsy specimens revealed the lymphoid cellular pattern of the infiltrate. Aspiration of sternal marrow, performed on March 25, 1947, showed no involvement whatsoever. A second aspiration of sternal marrow, performed on Jan. 21, 1948, revealed the over-all morphologic features of the bone marrow to be those of a highly malignant lymphoma or sarcoma. The pathologic diagnosis was advanced lymphosarcoma.

Autopsy Data.—The pathologic findings at autopsy were as follows: Generalized lymphosarcoma of the skin, enlarged periaortic nodes, hepatomegaly and splenomegaly, splenic infarcts with infarcts of the upper lobe of the left lung, generalized arteriosclerosis, icterus, papilloma of the bladder and nodular infiltration of the upper lobe of the right lung were observed. There was no evidence at autopsy, which included an examination of the head, to indicate that any organ or tissue was involved other than the skin and the bone marrow.

COMMENT

Since the early studies of the pathologic effects of compounds of mustard gas (β, β'-dichloroethyl sulfide) by Winternitz,[1] after World War I, there has been a gradually increasing interest in this field. Krumbhaar and Krumbhaar,[2] in 1918, although unaware of any acute cytotoxic alterations, did report on the autopsy findings in mustard gas (yellow cross gas) poisonings. In all their cases there were complicating severe pneumonias. These authors observed leukopenia in the peripheral blood, associated with atrophy and regeneration of the leukocytes from the fixed cells of the blood-forming tissues. Pappenheimer and Vance[3]

1. Winternitz, M. C.: Collected Studies on the Pathology of War Gas Poisoning, New Haven, Conn., Yale University Press, 1920.

2. Krumbhaar, E. B., and Krumbhaar, H. D.: The Blood and Bone Marrow in Yellow Cross Gas (Mustard Gas) Poisoning: Changes Produced in the Marrow in Fatal Cases, J. M. Research **40**:497-508, 1919.

3. Pappenheimer, A. M., and Vance, M.: The Effects of the Intravenous Injections of Dichloroethylsulfide in Rabbits with Special Reference to Its Leukotoxic Action, J. Exper. Med. **31**:71-94, 1920.

in 1920 reported results for rabbits after injection of β, β′-dichloroethyl sulfide. They felt that the leukopenia was the result of marrow atrophy and not of the peripheral destruction of granulocytes. Kindred,[4] using the methyl-bis compounds, showed that the small lymphocytes, erythroblasts, myelocytes and megakaryocytes are the most susceptible cells. The reticular and plasma cells are the most resistant. He also expressed the opinion that the reduction in the number of cells in the peripheral blood is a result of damage to the hemopoietic centers which in turn fail to replace cells lost from the circulating blood. Block[5] stated agreement with Kindred[4] on these findings. It was pointed out by Graef and associates[6] that factors such as the short life of lymphocytes (twelve hours or less) and the low reserve strength of lymphocytes also play a role in reducing the number of cells in the circulating blood.

Ten or fourteen days after the administration of nitrogen mustard a phase of regeneration begins. This is said to occur, during the first twenty-four hours, from the few susceptible cells not destroyed and, subsequently, from the reticular cells. According to Block[5] this process is similar to that described by Bloom[7] as occurring after roentgen irradiation to the entire body, except that regeneration proceeds more rapidly after nitrogen mustard therapy.

In our case of lymphosarcoma the process was apparently confined to the skin and the bone marrow. At least no other foci could be demonstrated even after a thorough search at autopsy. The disease advanced through the usual course of progression but was very sensitive to roentgen therapy. As the process spread to all regions of the body and the lesions became more refractory to further roentgen therapy, it was decided to give the patient a course of nitrogen mustard. The drug (methyl-bis [β-chloroethyl] amine) was administered in doses of 0.1 mg. per kilogram of body weight, on alternate days, for four doses.

The results, while conforming in general to the expected pattern, were extreme in regard to the severe depression of the hemopoietic system. The decided reduction of thrombocytes and the hemorrhage into the resolving lymphosarcomatous tissue was noted by Goodman and

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4. Kindred, J. E.: Histologic Changes Occurring in the Hemopoietic Organs of Albino Rats After Single Injections of 2-Chloroethyl Vesicants: Quantitative Studies, Arch. Path. **43**:253-295 (March) 1947.

5. Block, M.; Spurr, C. L.; Jacobson, L. O., and Smith, T. R.: Histopathologic Effects of Nitrogen Mustard Therapy upon Normal and Neoplastic Hemopoietic Tissues, Am. J. Clin. Path. **18**:671, 1948.

6. Graef, T.; Karnofsky, D. A.; Jager, V. B.; Krechesky, B., and Smith, H. W.: The Clinical and Pathologic Effects of Nitrogen and Sulfur Mustards in Laboratory Animals, Am. J. Path. **24**:1-47, 1948.

7. Bloom, W., cited by Block, Spurr, Jacobson and Smith.[5]

associates [8] and Jacobson and associates [9] in association with nitrogen mustard therapy of other lymphoblastomas. In retrospect we wonder if the generally accepted dose of this drug is not too large for patients of advanced years.

SUMMARY

A case of lymphosarcoma cutis is reported.

Only the bone marrow tissue and the skin were found to be involved.

The dose of nitrogen mustard (methyl-bis [β-chloroethyl] amine) was calculated on a basis of 0.1 mg. per kilogram of body weight administered intravenously on four alternate days.

Lethal outcome seemed to be precipitated by extreme lymphopenia, neutropenia and thrombocytopenia due to nitrogen mustard therapy.

It is suggested that smaller doses should be administered initially to elderly persons.

1219 Carew Tower (2) (Dr. McAfee).

8. Goodman, L. S.; Wintrobe, M. M.; Dameshek, W.; Goodman, M. J.; Gilman, A., and McLennan, M. T.: Clinical Experiences with the Use of Methyl-*Bis* (β-Chloroethyl) Amine Hydrochloride and *Tris* (β-Chloroethyl) Amine Hydrochloride for Hodgkin's Disease, Lymphosarcoma, Leukemia and Certain Allied and Miscellaneous Disorders, J. A. M. A. **132**:126 (Sept. 21) 1946.

9. Jacobson, L. O.; Spurr, C. L.; Guzman-Barron, E. C.; Smith, T.; Lushbaugh, C., and Dick, G. F.: Clinical Studies on the Effect of Methyl-Bis (Beta Chloroethyl) Amine Hydrochloride on Neoplastic Diseases and Allied Disorders of the Hemopoietic System, J. A. M. A. **132**:262 (Oct. 5) 1946.

CHRONIC LUPUS ERYTHEMATOSUS

Report of an Unusual Case with Concomitant Subcutaneous Edematous Nodes and Swellings; Historical Review

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A VERY unusual case of chronic discoid lupus erythematosus was recently observed. Present were the characteristic clinical features of this disorder; in addition, there were manifest subcutaneous nodes and edematous swellings of the face, head and neck. The latter may be observed in acute disseminated lupus erythematosis [1]; their occurrence in the chronic discoid form is extremely rare.

No mention is made of similar instances in the European literature. A few cases with aspects somewhat analogous to mine have been presented before dermatologic societies in this country. Irgang [2] and Arnold [3] described several more under the title of lupus erythematosus profundus. Study of the latter cases indicates that not a little confusion exists regarding the exact nosologic and etiologic evaluation of the nodes and swellings. This confusion extends to several of the more recent dermatologic texts and stems, undoubtedly, from the emphasis placed on the histologic features of the nodes themselves, features which Irgang and Arnold expressed the belief are of sufficient specificity to warrant a diagnosis of lupus erythematosus profundus even with the absence of the typical discoid lesions. Ormsby and Montgomery,[4] in their chapter on lupus erythematosus, stated, "Lupus erythematosus profundus is a deep nodular form described by Irgang and Bechet in which the lesions resemble Darier-Roussy sarcoid and erythema induratum and show histological features suggestive of sarcoid or other forms

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From the Dermatological Clinic, Boston Regional Office, United States Veterans Administration.

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1. Hebra, F., and Kaposi, M.: On Diseases of the Skin, Including the Exanthemata, London, The New Sydenham Society, 1875, vol. 4, pp. 21 and 32.

2. Irgang, S.: Lupus Erythematosus Profundus, Arch. Dermat. & Syph. **42**:97 (July) 1940.

3. Arnold, H. L.: Lupus Erythematosus Profundus (Kaposi-Irgang), Arch. Dermat. & Syph. **57**:196 (Feb.) 1948.

4. Ormsby, O. S., and Montgomery, H.: Diseases of the Skin, ed. 6, Philadelphia, Lea & Febiger, 1943, p. 890.

of hematogenous tuberculosis." Tobias [5] wrote, "Lupus erythematosus profunda is a deep variety and is probably related to sarcoid."

Clarification of the situation presented will be attempted on the basis of the clinical course, referential discussion and histopathologic observations in the case reported.

REPORT OF A CASE

A 27 year old veteran of World War II noticed an asymptomatic eruption on his nose and the adjacent portions of the cheeks for the first time in the early fall of 1942. Immediately after his induction, he had undergone intensive field training for three weeks, followed by eight consecutive months of kitchen duties. At the end of the latter period, during which he was exposed less than normally to the sun and the elements, the cutaneous disease appeared. There was no history of

Fig. 1.—Lesions of chronic discoid lupus erythematosus on nose and face. A large, edematous node may be seen above the outer left canthus, involving the left eyebrow and the subcutaneous tissues above. Overlying the upper portion of the node was a discoid patch which, with underlying nodal tissue, was removed for biopsy.

trauma. The only therapy up to 1944 had been the local application of calamine lotion.

In April 1944, he received an intramuscular injection of an insoluble bismuth compound. The continuation of this treatment was interrupted for about six weeks by his transfer to England, where, after about seven additional injections of bismuth compound, the eruption entirely cleared. His skin remained clear until September 1946, four months after separation from the Army. In this interim, there was no abnormal exposure to the sun or local trauma. On the reappearance of the eruption at its original sites, the patient consulted a local physician, who

5. Tobias, N.: Essentials of Dermatology, ed. 2, Philadelphia, J. B. Lippincott Company, 1944, p. 44.

prescribed penicillin ointment. The latter was applied twice daily up to Nov. 26, 1946, when the patient visited for the first time the medical clinic of the Boston regional office of the Veterans Administration. A diagnosis of chronic discoid lupus erythematosus was made, and 1 cc. of insoluble bismuth subsalicylate injection was administered. The patient returned to his local physician with authorization for the continuance of treatment with the parenterally administered bismuth compound. A total of twenty injections was given before disappearance of the eruption was effected in May 1947. The patient returned to the skin clinic in Boston on May 5, 1948, with the history of recurrence of the eruption dating back to January 1948. From May to August 1948 he took orally about 150 Gm. of bismuth sodium triglycollamate (bistrimate®), without any effect.

The patient again returned to the clinic on Nov. 9, 1948. From August on he had received no medication. His work was indoors, with no exposure to the sun. There was no history of recent infections or of local trauma. In addition to the old lesions on his nose and the adjacent portions of the cheeks, new lesions had

Fig. 2.—Disappearance of node over left eye and pronounced improvement of lesions of chronic lupus erythematosus on nose and face. The photograph was taken after one month of oral treatment with low doses of sodium para-aminobenzoate.

appeared early in September over, lateral to and above the left eyebrow. Similar patches had simultaneously appeared over the bony protuberance below the outer third of the left eye and in the left concha. They gradually grew in extent. At the same time the patient noticed pea-sized "swellings" "under" and beyond these new lesions. In early October a large "swelling" appeared on the right side of the neck just lateral to and over the right mandibular angle. On November 2 a large "swelling" appeared on the top of the scalp.

Physical examination revealed discoid patches of lupus erythematosus covering at least three fourths of the bridge and sides of the nose. They extended only slightly on the right cheek but spread diffusely on the left under the eye, becoming much wider at and beyond the outer canthus. Above and lateral to the outer third of the left eyebrow was a patch 1 by 0.5 cm., irregularly outlined. Underlying the latter and extending about 1 cm. laterally was a semihard, slightly tender, ill defined, filbert-sized subcutaneous tumor. Beneath the patch below the left outer canthus

was a slightly smaller subcutaneous node. On the left cheek, just below its junction with the lower rim of the ear, was an ill defined semihard, tender, pea-sized node with overlying normal skin. (The patient stated that the last-mentioned lesion had appeared about two months previously.) On the neck, starting just below the lower rim of the right ear and extending down to about 0.5 cm. below and for about 0.25 cm. over the jaw was an oval, almond-sized, ill defined, tender, somewhat doughy, subcutaneous tumor with overlying normal skin. On the vertex of the scalp, 8 cm. posterior to the anterior hair line, was a walnut-sized, tender, ill defined subcutaneous "swelling" with normal overlying skin extending 0.375 cm. above the surface of the scalp. The subcutaneous nodes or tumors were definitely

Fig. 3.—Low power view (× 18) of superficial lesion manifesting typical changes of lupus erythematosus. Visible are the dense lymphocytic infiltrates in the middle and deep portions of the corium; hematoxylin and eosin stain.

not lymph nodes and clinically resembled lesions not uncommonly referred to as the Darier-Roussy sarcoid.

The temperature, results of studies of the blood, sedimentation rate, serum albumin-globulin ratio, results of urinalysis and roentgenograms of the lungs were normal. The serologic test for syphilis (Hinton) gave negative reactions.

Histologic Examination.—Since the taking of only one biopsy specimen was permitted, a strip of skin, 6 by 2 by 1 mm., from the erythematous lesion, with a piece of underlying tumor tissue, 4 by 3 by 2 mm., was excised just above the left eyebrow. Pathologic changes typical of chronic lupus erythematosus were present in the epidermis and upper portion of the corium. Patchy lymphocytic

infiltrates were visible in the middle and lower parts of the corium. In the latter regions, the infiltrates were larger and contained small and equal numbers of histiocytes, plasma cells and neutrophils. As the inflammatory changes extended into the hypoderm and subcutaneous fat, they were more diffuse and in places entirely replaced the fat tissue. Although still predominantly lymphocytic, a greater proportion of histiocytes, plasma cells and neutrophils were visible. Some of the histiocytes were definitely foamy. Occasional fibroblasts and a rare eosinophil were observed. Perivascular infiltrates composed of lymphocytes, neutrophils and occasional fibroblasts surrounding and in places invading proliferative vessel

Fig. 4.—Higher power view (× 100) of the superficial tissue overlying a node shown in figure 3. Typical changes of chronic discoid lupus erythematosus are evident; hematoxylin and eosin stain.

walls were seen in the deep part of the corium and the subcutaneous fat. The histologic changes in the latter region was analogous to Wucher (fat replacement) atrophy. Walter F. Lever,[6] who also examined the slide, stated that the changes in the superficial part of the specimen were consistent with those of chronic lupus erythematosus but that he had never seen similar changes in the deep part of the corium and the fat as concomitants in this entity. His opinion was that these

6. Lever, W. F.: Personal communication to the author.

changes were of no diagnostic import and represented only a nonspecific inflammation. The underlying muscle tissue was normal, and anything remotely suggestive of a sarcoid reaction was absent.

Clinical Course.—After the biopsy, the patient was instructed to take orally 1.5 Gm. sodium para-aminobenzoate[7] four times a day. The dose was kept purposely low because the patient lived far from the clinic. Ten days later the sub-

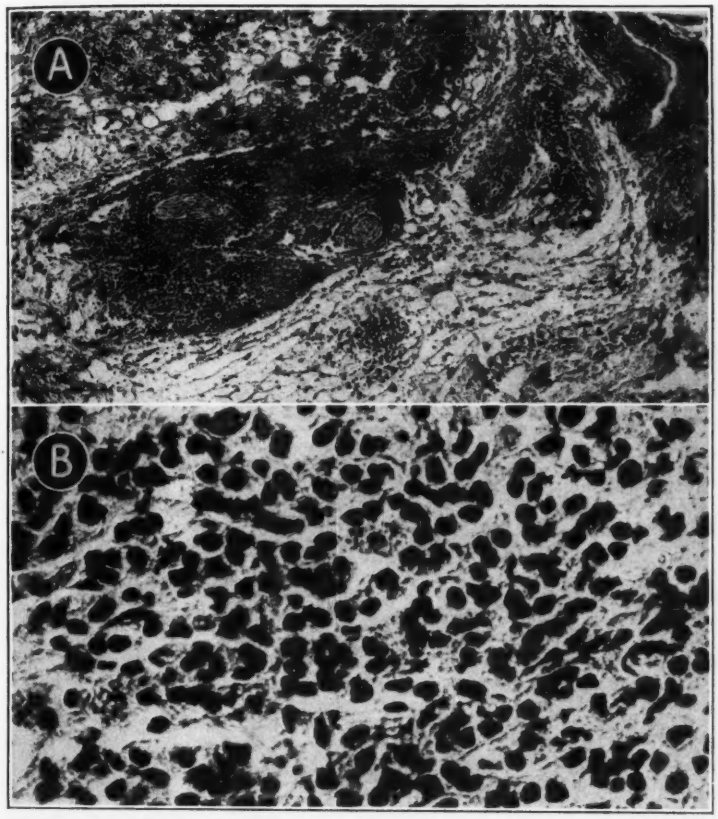

Fig. 5.—*A*, low power view (× 20) of nodal tissue, showing the deep portion of the corium and the hypoderm. Large agglomerations of lymphocytes may be seen in the deep part of the corium, with invasion and in places replacement of the fat tissue by infiltrate; hematoxylin and eosin stain. Proliferation of vessel walls and perivascular infiltrates are visible. *B*, higher power photomicrograph of a predominantly lymphocytic infiltrate in the deep portion of the corium. Occasional histiocytes and plasma cells are present; hematoxylin and eosin stain.

7. Zaraforetis, C. J. D.; Curtis, A. C., and Grekin, R. H.: The Effects of Para-Aminobenzoic Acid in Lupus Erythematosus: A Preliminary Report, Univ. Hosp. Bull., Ann Arbor **13**:122, 1947.

cutaneous nodes were neither visible nor palpable. The small tumors on the head and right side of the neck had receded to one-third their previous size. The erythematous patch partly overlying the node above the left eye was replaced by a faintly pigmented residual area. Similar changes were visible below the left eye. The chronic and infiltrated lesions on the nose and adjacent parts of the cheeks were flatter, paler and slightly pigmented. These, with the exception of a slightly elevated erythematous ridge about 1 by 0.25 cm. on the bridge of the nose, were replaced by faint pigmentation, barely perceptible superficial atrophy and slight

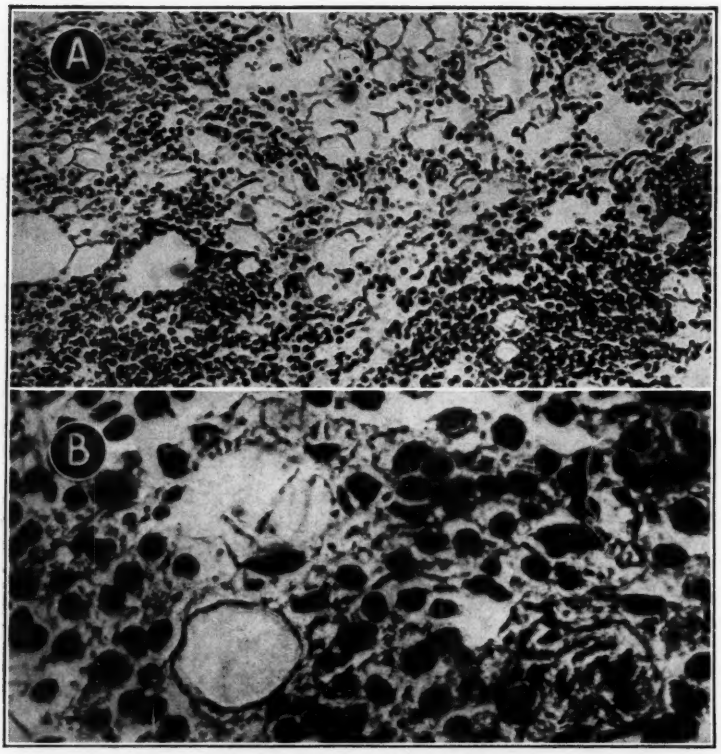

Fig. 6.—*A*, infiltrate (× 100) in tissue of node diffusing between and replacing the fat globules of the hypoderm; hematoxylin and eosin stain. Wucher atrophy (fat replacement atrophy) is prominent. *B*, high power (× 400) view of infiltrate in fat tissue. Although predominantly lymphocytic, it is less compact and composed of more histiocytes, some of which have a foamy appearance. Equal numbers of plasma cells and neutrophils are present. A rare eosinophil is visible; hematoxylin and eosin stain.

enlargement of follicular orifices after one month of paraaminobenzoate therapy. Nowhere evident were the swellings and nodes, which the patient stated had disappeared ten days previously. Evidently all manifestations, cutaneous and subcutaneous, had receded concomitantly. Blood counts and results of urinalysis

were within normal limits. The patient stated that equally good results were apparent after two and one-half weeks' treatment with oral administrations of sodium paraaminobenzoate as had previously occurred after five months of weekly intramuscular injections of insoluble bismuth.

HISTORICAL REVIEW

Clinical and Histologic Aspects.—Practically no mention is made in any of the modern dermatologic texts of subcutaneous nodes or swellings as such accompanying the characteristic lesions of chronic lupus erythematosus. In the several instances in which they were described, there was a misconception as to the particular form of lupus erythematosus in which these nodules may form a part of the composite picture. For example, Pusey,[8] in the various editions of his text, under the subheading of "nodular erythematous lupus," wrote, "Crocker describes a nodular form of erythematous lupus in which, perhaps in association with typical discoid patches, numerous round or oval elevated nodules from the size of a hemp seed to that of a bean appear scattered over the upper part of the face." Evidently Pusey himself had never encountered them. Crocker, however, like Pusey, never having seen the nodes, credited Kaposi [1] with the first description of "subcutaneous, deeply seated, doughy and tender nut sized nodules which appear (in lupus erythematosus) while the skin over them is still normal." [9] Kaposi, on the other hand, in his at the time comprehensive clinical and anatomic descriptions of chronic discoid lupus erythematosus, nowhere mentioned nodes or swellings as possible accompaniments of this form. His only description of them was under the "concomitant symptoms" of disseminated lupus of the acute type, which he designated "lupus erythematosus disseminatus et aggregatus." [1]

The first reference to subcutaneous nodules in chronic lupus erythematosus was in a case presented before the New York Dermatological Society by Kingsbury.[10] Subsequent reports [11] were similarly of cases presented before dermatologic societies. In all there were present the typical lesions of chronic lupus erythematosus with additional subcutaneous nodes or plaques and overlying normal skin situated on various

8. Pusey, W. A.: The Principles and Practice of Dermatology, ed. 4, New York, D. Appleton & Co., 1924, p. 393.

9. Crocker, H. R.: Diseases of the Skin: Their Description, Pathology, Diagnosis, and Treatment, ed. 2, Philadelphia, P. Blakiston, Son & Co., 1893, p. 531.

10. Kingsbury, J.: Sarcoid and Favus, J. Cutan. Dis. **36**:533, 1918.

11. (*a*) Fordyce, J. A.: Lupus Erythematosus with Nodular Lesions Suggesting Sarcoid, Arch. Dermat. & Syph. **11**:852 (June) 1925. (*b*) Oliver, E. L.: Lupus Erythematosus: Sarcoid, ibid. **12**:150 (July) 1925. (*c*) Chargin, L.: Erythematosus of Face and Boeck's Sarcoid of the Arms, ibid. **36**:458 (Aug.) 1937.

portions of the body. In Kingsbury's case [10] the lesions were on the arms; in Fordyce's,[11a] on the face; in Oliver's,[11b] on an arm and a buttock, and in Chargin's,[11c] on the arms. In every instance a diagnosis of lupus erythematosus and sarcoid was made, with the sarcoid designated as of the Darier-Roussy type by either the presenter or the discusser. Although in Chargin's case the clinical diagnosis was at first lupus erythematosus of the face and Boeck's sarcoid of the arms, it was later changed [12] to lupus erythematosus of both areas, the later diagnosis being based on the subsequent histologic changes in tissue removed from a thickened and erythematous lesion on one of the arms. For purposes of discussion, this last-mentioned case may therefore be eliminated, since it differed clinically and histologically from those previously and subsequently reported.

In none of the preceding cases were specimens taken and histologic examinations carried out. This is understandable because of the rarity of such procedures at the time. With most dermatologists then of the belief that both lupus erythematosus and sarcoid were essentially tuberculous, it was logical that the appellation Darier-Roussy sarcoid be applied clinically to the rare instances in which additional subcutaneous (separated) lesions might accompany lupus erythematosus. With present day diagnostic methods such a procedure is impossible. Omitting the more recent etiologic considerations of both these diseases, it is accepted that a definite diagnosis of sarcoid or sarcoidosis cannot with certainty be made without microscopic evidence.[13] Considerable doubt has furthermore been cast on the very existence of the entity Darier-Roussy sarcoid. Lever and Freiman,[14] in a recent extensive review of the European and American literature, concluded that all cases reported as of Darier-Roussy sarcoid in which subcutaneous nodes but no cutaneous or systemic lesions of sarcoidosis were present were not instances of this entity, since in none did the microscopic picture resemble sarcoidosis. They advise, from a microscopic standpoint, at least, the discarding of the term Darier-Roussy sarcoid. On alinement of these observations, it may be categorically assumed that the Darier-Roussy sarcoid was not present in the cases presented as lupus erythematosus and sarcoid, in which the ostensible sarcoid lesions were manifest as subcutaneous nodes and/or small subcutaneous tumors. These conclu-

12. Chargin, L., and Wolf, C.: Lupus Erythematosus of Face and Boeck's Sarcoid of the Arms, Arch. Dermat. & Syph. **40**:499 (Sept.) 1939.

13. Michelson, H. E.: Sarcoidosis: A Review and Appraisal, J. A. M. A. **136**:1034 (April 17) 1948. Freiman, D. G.: Sarcoidosis, New England J. Med. **239**:664, 1948.

14. Lever, W. F., and Freiman, D. G.: Sarcoidosis, Arch. Dermat. & Syph. **57**:639 (April) 1948.

sions may be applied not only to the last-mentioned cases but also to those instances in the authoriative texts previously referred to that mention the association [15] of sarcoid and lupus erythematosus.[5]

In more recent studies, Irgang [2] and Arnold [3] introduced a new term, lupus erythematosus profundus, as a diagnostic designation for the type of case under discussion. Arnold's appellation was lupus erythematosus profundus (Kaposi-Irgang), based on Kaposi's supposedly first description of specific histopathologic features of the subcutaneous nodes that may rarely accompany a chronic lupus erythematosus and Irgang's first introduction of the concept in the American literature. Irgang's patient presented presumptive lupus erythematosus lesions on the right cheek and a flat plaque with freely movable overlying normal skin on the upper part of the back. Arnold's in 1943 was treated for lupus erythematosus of the scalp and in 1945 manifested atrophic residual areas on the scalp and painless, nontender, rubbery, hard, sharply outlined, movable subepidermal tumors with overlying normal skin of the face. In both, the histopathologic features at biopsy were seen to be essentially similar; the changes were not dissimilar to those observed in my case. After reviewing the cases of Oliver [11b] and Fordyce [11a] and referring to several cases presented before the Vienna Dermatological Society by Kren [16] and Oppenheim [17] in 1912 with lesions which Irgang expressed the belief were similar to those observed in his case, Irgang postulated three types of lupus erythematosus, a superficial, a median and a deep, with the latter two essentially tuberculous, clinically manifesting themselves as Boeck's sarcoid, the Darier-Roussy sarcoid or erythema induratum. Histologically, on the basis of the microscopic changes in his own patient, Irgang expressed the belief that a diagnosis of lupus erythematosus profundus could be made in a case with subcutaneous nodes or plaques as the only presenting symptoms. As an example, the case of a patient of Michelson's [18] who was presented before the Minnesota Dermatological Society for diagnosis (sarcoid?) was cited.

The cases of Fordyce [11a] and Oliver [11b] have already been dealt with. A detailed examination of those reported by Kren,[16] Oppenheim [17] and Michelson [18] is therefore necessary for a correct evaluation of the term lupus erythematosus profundus as conceived by Irgang. Kren's patient was a 73 year old woman with lupus vulgaris of the nose and bluish red nodules on the sides of the fingers; the diagnosis clinically and histo-

15. Footnote 4, p. 873.

16. Kren, O.: Case Presentation, Vienna Dermatological Society, Arch. f. Dermat. u. Syph. **112**:391, 1912.

17. Oppenheim, M.: Case Presentation, Vienna Dermatological Society, Arch. f. Dermat. u. Syph. **115**:847, 1913.

18. Michelson, H. E.: A Case for Diagnosis (Subcutaneous Sarcoid?), Arch. Dermat. & Syph. **22**:530 (Sept.) 1930.

logically was lupus vulgaris erythematoides. Oppenheim's, in which there was no biopsy, was presented as lupus erythematosus profundus of Brocq. In the discussion of it [17] Scherber stated that a similar case had been previously observed in Finger's clinic and that histologically it had exhibited the findings of lupus vulgaris erythematoides through the entire section. At this point, however, it is necessary to clarify the term *"lupus érythémateux profond"* as it was employed by Brocq.[19] Brocq originally designated by this appellation lesions deeply infiltrative, cartilaginous and clinically somewhat analogous to discoid lupus erythematosus to prove his contention that lupus erythematosus was tuberculous but later, according to Pautrier,[20] discarded the term in deference to his changed conception of the true nature of these lesions, namely that they were manifestations of lupus vulgaris. Bechet [21] emphasized this point when he called attention to the omission of *"lupus érythémateux profond"* from Brocq's chapter on lupus erythematosus in his "Traité élémentaire de dermologique pratique." From a clinical standpoint, therefore, it is obvious that none of the European cases that Irgang quoted resembled those with lupus erythematosus (chronic) lesions and additional subcutaneous nodes encountered in this country. Obviously, it is impossible to employ them as the basis for the logical diagnostic evaluation of the cases found here. Histologically, a similar deduction may be drawn from Michelson's case, in which were presented numerous subcutaneous plaques on the cheek, arms and hips but nowhere any cutaneous manifestations of chronic lupus erythematosus. Microscopic sections of one of the lesions presented diffuse as well as perivascular infiltrates of lymphocytes and neutrophils with pronounced Wucher atrophy (fat replacement atrophy). Irgang [2] interpreted these findings as specific for the deep form of lupus erythematosus, or lupus erythematosus profundus, because of their similarity to those in his own case. Yet Montgomery, in the discussion of Michelson's case,[18] remarked that the inflammatory reaction was nonspecific and did not permit a diagnosis.

The affixing of Kaposi's name to lupus erythematosus profundus on the basis of his supposedly first histopathologic description of the subcutaneous nodes in chronic lupus erythematosus is similarly unfortunate, since it does not bear scrutiny. Arnold,[3] in support of the linking of Kaposi's name with the entity in question, quoted from several editions of Kaposi's text:

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19. Brocq, L.: Sur la nature du lupus érythémateux, Rév. gén. de clin. et de thérap. **9**:113, 1895.

20. Pautrier, L. M.: Lupus erythematosus, in Darier, J., and others: Nouvelle pratique dermatologique, Paris, Masson & Cie, 1936, vol. 3, p. 747.

21. Bechet, P.: Lupus Erythematosus Hypertrophicus et Profundus, Arch. Dermat. & Syph. **45**:33 (Jan.) 1942.

Thus the process begins at one time in the upper layers and in the neighborhood of the blood vessels surrounding the sebaceous glands and their ducts (red elevated macules) and at another time in the deep layers in the neighborhood of the vascular network belonging to the sweat glands and the fat lobules (firm, oedematous nodules), and spreads throughout all the skin layers and tissues.[22]

The "process" referred to by Kaposi dealt, however, with microscopic inflammatory reactions and infiltrates of the macules and edematous nodules of the disseminated lupus erythematosus, considered today to be of the acute exanthematous type. The quotation was taken piecemeal from the context of Kaposi's chapter on lupus erythematosus and conveys an entirely different impression from that intended by Kaposi. For, in the edition which I have of his text,[1] shortly prior to the aforementioned transcription, Kaposi wrote, under "Symptomatology," the following remarks:

Lupus erythematosus always becomes developed in a two fold manner; first, as characteristic large discs which I shall call the discoid form; secondly, as disseminated spots of the character described which I shall call lupus erythematosus disseminatus et aggregatus. . . . In the first case, lupus erythematosus remains for a long time quite local. . . . In the second case, the disease usually becomes general, and then in the course of a few days or one or two weeks, hundreds of spots of erythematous lupus become distributed over the trunk, on the flexor and extensor surfaces of the fingers, in the palm and back of the hand, on the arms, thighs, legs, elbows, knees, both back and front and in fact over almost the whole body.

From "Concomitant Symptoms," I quote these statements:

The symptoms which may be associated with an actue or subacute eruption of lupus erythematosus are . . . 1. Nodules of the size of hazel nuts or walnuts which are situated deeply or in the subcutaneous cellular tissue are painful spontaneously, feel of the consistence of firm dough, are tender and are covered by skin of a normal color, but pushed forward by them.

Under "Anatomy," prior to the excerpt taken by Arnold from Kaposi's text, the following appears:

In the stage characterized by the presence of the deep seated painful oedematous nodes mentioned, which so often precedes the development of the eruptive spots of lupus, there exist cellular infiltrations in the meshes of the connective tissue etc.

It is evident, therefore, that nowhere did Kaposi mention nodes as concomitant symptoms of chronic lupus erythematosus.

To recapitulate, extremely few cases of chronic lupus erythematosus with concomitant subcutaneous nodes or small subcutaneous tumors have to date been reported. The early ones were diagnosed as lupus erythematosus and Darier-Roussy sarcoid. The absence of biopsy speci-

22. Kaposi, M.: Pathologie und Therapie der Hautkrankheiten, in Vorlesungen für praktische Aerzte und Studirende, ed. 2, Vienna, Urban & Schwarzenberg, 1883, p. 642; ed. 5, 1899, p. 749.

mens and histologic examinations in these cases, together with the possibility that the entity commonly designated Darier-Roussy sarcoid is nonexistent, renders the second portion of the diagnosis improbable. The term lupus erythematosus profundus was first applied in this country as a diagnosis for similar cases and was based on supposedly "specific" microscopic changes in the nodes themselves. Originally employed in Europe with the mistaken conception of a tuberculous etiology of lupus erythematosus, it had been discarded because cases previously presented as lupus erythematosus profundus (Brocq) were later definitely diagnosed lupus vulgaris erythematoides. The microscopic picture in the 3 cases in which biopsies were done (including mine) were fundamentally similar. The specimens presented changes of an entirely nonspecific nature, changes which did not permit a definite histologic diagnosis. Certain histopathologic features of some phase of such unrelated entities as erythema nodosum,[23] erythema induratum [24] and Weber-Christian disease [25] were evident. Clinicaliy, nodes or subcutaneous tumors may be present in all three. It is evident, therefore, that a diagnosis of a median or deep form of lupus erythematosus based on the presence of and the histologic changes in the additional subcutaneous nodes or tumors themselves is an impossibility The term lupus erythematosus profundus is obviously a misnomer and should be discarded. If employed at all, it should be in the sense in which Bechet [21] used it. Under the title of lupus erythematosus hypertrophicus et profundus, he reported 2 cases of lupus erythematosus with raised and greatly indurated lesions to illustrate their clinical atypicality and pronounced resistance to treatment. Previously recognized as a variant of chronic discoid lupus erythematosus, this type was described by Sulzberger and Wolf [26] as a hyperkeratotic discoid type with a grayish, verrucous, worm-eaten, centrally depressed area and red, elevated, cordlike border suggesting epithelioma or hypertrophic lichen planus. Andrews [27] employed the term in a similarly correct manner.

The case in this report was presented not merely for its clinical and histologic interest but also for demonstration of the dramatic and rapid results obtained with the empiric low dose of sodium paraaminobenzoate administered orally. I do not intend to generalize on the beneficial effects

23. Lever, W. F.: Histology and Histopathology of the Skin, Boston, The Author, 1947, p. 42.

24. Lever,[26] p. 34. Montgomery, H.: Atlas of Dermal Pathology, Washington, D. C., Registry Press, 1948, p. 89.

25. Lever,[26] p. 25.

26. Sulzberger, M. B., and Wolf, J.: Dermatologic Therapy in General Practice, Chicago, The Year Book Publishers, Inc., 1940, p. 494.

27. Andrews, G. C.: Diseases of the Skin for Practitioners and Students, ed. 3, Philadelphia, W. B. Saunders Company, 1946, p. 588.

obtained. My associates and I are not certain of their permanency. In several other cases the results have been good but much slower. In these last-mentioned cases, the patients manifested clinical improvement only after treatment with 15 to 20 Gm. of the compound daily. In 3 more, including a case of the type described by Bechet and by Sulzberger and Wolf there had been, to the time of writing, no manifestation of improvement. In 1, the condition of the patient became worse.

The occurrence in this patient of nodes and subcutaneous edematous swellings, simultaneously with the development of new chronic lupus erythematosus lesions and extension of the old ones, was similarly striking. With the present accepted belief of the identity of the chronic and the acute and subacute disseminated forms of lupus erythematosus, it is a not implausible assumption that the nonspecific edematous subcutaneous nodes originally described by Kaposi as an accompaniment of the acute and subacute disseminated forms may in rare instances be encountered with chronic discoid lupus erythematosus also.

SUMMARY AND CONCLUSIONS

An unusual case of chronic discoid lupus erythematosus with concomitant subcutaneous nodes and edematous swellings is reported, in which empirically employed low doses of orally administered sodium paraaminobenzoate effected rapid disappearance of all lesions.

The few essentially analogous cases previously described were presented either as chronic lupus erythematosus and Darier-Roussy sarcoid or as lupus erythematosus profundus. No accepted evidence, such as biopsy specimens and histologic examination, was offered to substantiate the second portion of the first diagnosis. With regard to the second diagnosis all related historical, clinical and histologic facts indicate that the term lupus erythematosus profundus for the cases reported is a misnomer and should be discarded.

It is not improbable that, since some of the cutaneous lesions of chronic lupus erythematosus and the additional subcutaneous nodules and swellings appeared simultaneously in the case reported, the same at present unknown etiologic factor was responsible for both.

Dr. J. D. Houghton, pathologist of the West Roxbury Veterans Administration Hospital, cooperated in this study.

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A THEORY OF THE PATHOGENESIS OF ORDINARY HUMAN BALDNESS

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BALDNESS in men is such a common occurrence that it has almost come to be accepted as a normal phenomenon. This view has been encouraged by the attributing of the condition either to irrevocable heredity or to the ubiquitous condition of seborrhea. Understandably, however, much thought and investigation have been expended in an attempt to comprehend and reverse this blow to masculine pride. Work on the subject has been carried out almost exclusively by dermatologists. A review of the most authoritative present day dermatologic textbooks indicates, however, that the problem is still far from being solved.

We, as psychiatrists, were initially drawn to this problem by observations on facial expression. These observations, together with certain significant contributions to the literature which were apparently hitherto overlooked, led to the formulation of what is offered as a comprehensive explanation of the pathogenesis of ordinary human baldness.

CRITICAL REVIEW OF THE LITERATURE

The literature dealing with the problem of ordinary human baldness is extraordinarily large. A careful review of the various hypotheses concerning the etiology of this condition reveals that the several factors which have been thought to cause or to contribute to baldness can be divided into five more or less distinct categories.

Seborrhea.—Practically all textbooks on dermatology [1] mention seborrhea as one of the etiologic factors in ordinary alopecia. It is difficult to ascertain the exact origin of this hypothesis. Sabouraud was

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1. (*a*) Becker, S. W., and Obermayer, M. E.: Modern Dermatology and Syphilology, ed. 2, Philadelphia, J. B. Lippincott Company, 1947. (*b*) Ormsby, O. S., and Montgomery, H.: Diseases of the Skin. ed. 6, Philadelphia, Lea &

noteworthy as a strong advocate of this idea, and his students continued the teaching that baldness was "caused" by seborrhea. Among the more recent works on this subject, Agnes Savill's book [2] presented this view most clearly. She wrote, "In a case of severe seborrhea oleosa the usual course is at first rapid and then a gradual march toward the complete baldness with a stretched glossy skin which is so frequently seen in men." [3] And, again, "From the above description of the usual course of seborrhea oleosa in men, it might be gathered that when once seborrhea begins on the scalp there is no hope for the young man; that sooner or later his scalp must become entirely bald with the exception of the ring of hair which even in the worst cases appears to be left at the occiput and above the ears." [4]

Comment: The seborrhea hypothesis, though representing at present perhaps the most widely held view concerning the etiology of baldness, seems a thoroughly inadequate explanation of the problem, as it cannot account for its specific distribution. Though seborrhea is just as severe over the occiput and the eyebrows as it is on the top of the head, in ordinary human alopecia the hair is never lost from these areas. Similarly, severe seborrhea may be found in many men who never lose their hair. J. B. Hamilton,[5] in his excellent investigation on the role of male sex hormones in baldness, demonstrated conclusively that seborrhea is one of the results of male sex hormone stimulation. This is in harmony with well known clinical observations concerning the development of acne and the presence of greater oiliness in the skin and scalp of boys at puberty. Baldness and seborrhea frequently coexist, but this fact does not warrant any conclusion concerning a causal relationship between them.

The Role of Hormones.—The effect of internal secretions on the development of alopecia is well established. Hippocratic baldness in women is a very rare occurrence. McCarthy [6] cited a case described

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Febiger, 1943. (*c*) Sulzberger, M. B., and Wolf, J.: Dermatologic Therapy in Medical Practice, Chicago, The Year Book Publishers, 1940. (*d*) Sutton, R. L., and Sutton, R. L., Jr.: Synopsis of Diseases of the Skin, St. Louis, C. V. Mosby Company, 1942. (*e*) McCarthy, L.: Diagnosis and Treatment of Diseases of the Hair, St. Louis, C. V. Mosby Company, 1940. (*f*) Galewsky, E.: Erkrankungen der Haare und des Haarbodens, in Jadassohn, J.: Handbuch der Haut- und Geschlechtskrankheiten, Berlin, Julius Springer, 1932, vol. 13.

2. Savill, A.: The Hair and the Scalp, ed. 3, Baltimore, Williams & Wilkins Company, 1945.

3. Savill,[2] p. 99.

4. Savill,[2] p. 100.

5. Hamilton, J. B.: Male Hormone Stimulation Is Prerequisite and an Incitant in Common Baldness, Am. J. Anat. **71**:451-480 (Nov.) 1942.

6. McCarthy,[1e] p. 591.

by Fasal of a female patient with infections of the ovaries who developed masculine hair on the face and at the same time became bald. In older women, years after the menopause, masculine characteristics frequently develop. These include changes in the distribution of body fat, growth of facial hair and sometimes mild degrees of baldness. J. B. Hamilton's work, previously referred to, is relevant and may be briefly summarized as follows: In prepubertally castrated men, he found no loss and not even a normal recession of hair in the frontoparietal region as seen in adult men. He noted a much reduced sebaceous secretion in the scalp and little or no dandruff. After castration between the ages of 14 and 19 years, alopecia was found to be absent or incomplete; it was variable in degree when castration occurred between 20 and 43 years. Hamilton administered testosterone propionate to a group of eunuchoid and castrate men. He found that he could produce alopecia in some of them. ("Since alopecia does not progress spontaneously in castrate and eunuchoid men, it is no mere coincidence that pronounced loss of hair occurred in four men with testicular insufficiency when they received androgenic stimulation.") Stopping the treatment brought about a cessation in the progress of the alopecia. With the administration of male sex hormone, there was also a concomitant increase in sebaceous secretions and in the amount of dandruff; in other words, "seborrhea" developed. Finally, Hamilton, too, reported on the occurrence of baldness in women with masculinizing tumors.

Comment: The data just reported appear to provide conclusive evidence that male sex hormone stimulation is a prerequisite for the development of ordinary human baldness. The simple observations that baldness does not ordinarily appear in females and occurs in males only after puberty are in accord with this. However, since not all men become bald, it is clear that hormonal stimulation is only one of the prerequisites. The additional factors which in the presence of male hormone stimulation lead to the development of alopecia remain to be explained.

Tightly Fitting Hats.—Benjamin L. Dorsey [7] strongly advocated the idea that the wearing of hats causes alopecia. He referred to ordinary human baldness as "traumatic baldness" because he believed that tightly fitting hats over a long period of time compress and traumatize the temporal artery and vein on each side of the head. "However, the most elastic arteries must succumb in time to hat pressure, just as a garden hose, when repeatedly kinked at a certain point, will at last fail to resume its normal diameter. Though it may take many years, in

7. Dorsey, B. L.: Baldness: Its Cause and Prevention, Los Angeles, De Vorss & Co., 1939.

the end the hat band must win."[8] He explained the role of heredity in baldness as ". . . simply that of a predisposing factor; that is, the victims have inherited conical or oval-shaped heads; those that escape it have inherited long narrow heads; and as both inheritances may occur in the same family one brother may be bald and the other not."[9]

Comment: The chief objection to this hypothesis is the fact that many men who never wear hats become bald. There is no evidence that baldness in men who do not wear hats is in any way different from the baldness that occurs in those who do. It seems doubtful that the majority of men who wear hats wear them tightly enough to produce pathologic changes in the temporal artery or vein even when the pressure is exerted over a long period of time. In addition, Dorsey attempted to account for the occurrence of alopecia in men only by suggesting that only men wear tightly fitting hats. The experiments of Hamilton leave little doubt that hats do not account for baldness.

Heredity.—Herbert Rattner[10] wittily concluded his paper on ordinary human baldness by stating that "the man who would avoid baldness had better use greater care in the choice of his ancestors." Similarly, most other workers in this field feel that heredity plays a very important role. Hamilton,[5] though concentrating on the role of male sex hormones, also considered the effect of genetic factors. His comments are relevant:

"One can conclude, further, that a genetic tendency to baldness, although dependent for fulfillment on androgenic stimulation, is not expressed simply and solely by this mechanism, since quantities of androgens far greater than those that incite alopecia in some patients exerted no such effect in other patients, especially in some individuals whose pedigree indicated no genetic susceptibility to baldness. It seems noteworthy that androgenic incitation of alopecia is an example in the human of a mechanism whereby a genetic predisposition may be realized."

Comment: We are not in a position to evaluate the importance of genetic predisposition in the etiology of ordinary alopecia. It appears, however, from the available evidence that it plays a significant role.

Tension or Stretching of the Scalp.—In 1903, Moriz Schein published two papers[11] in which he suggested that scalp tension was the crucial etiologic factor in the production of ordinary human baldness.

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8. Dorsey,[7] p. 94.

9. Dorsey,[7] p. 95.

10. Rattner, H.: Ordinary Baldness, Arch. Dermat. & Syph. **44**:201-213 (Aug.) 1941.

11. (*a*) Schein, M.: Ueber die Entstehung der Glatze, Wien. klin. Wchnschr. **16**:611-615 (May 21) 1903; (*b*) Zur Frage der Entstehung der Glatze, ibid. **16**:968-970 (Aug. 20) 1903.

More recently, M. Wharton Young[12] advanced similar ideas and attempted to substantiate them with some interesting experimental work.

In his first paper, Schein reviewed the then current theories of baldness, that it was due to (1) seborrhea, (2) cutting of the hair and (3) hats. As none of these explained specific distribution, it was suggested that local factors must be operative. Schein expressed the belief that contraction of the epicranial muscles reduced the circulation of blood and lymph by compressing the skin and connective tissues overlying the galea aponeurotica onto the galea. He proposed that it is not alopecia per se which is inherited but the shape of the skull favoring its development and concluded that the nourishment of skin and hair is the determining factor in the etiology of baldness. The difference between men and women in relation to alopecia was explained by a differential development of the epicranial muscles. Just as the general bodily musculature is more highly developed in men, so is the musculature of the epicranium. Schein stated further that the heads of men are generally larger and more convex on top than those of women; these factors favor the development of greater tension over the top of the head in men.

In another paper published a few months later, Schein referred to the work of J. Pohl-Pincus, who many years earlier (1875) had come to the same conclusions by a different approach. Whereas Schein relied on anatomic and mechanical considerations, Pohl-Pincus had approached the problem from a histologic standpoint. Most of Schein's second paper consists of quotations from the early work of Pohl-Pincus, who found a tight compression of tissue spaces in the scalps of bald men and attributed the loss of hair to this. This was in contrast with the finding that the scalp tissues over the galea in women appear loose on histologic examination. The looseness of the connective tissues of women was compared by Pohl-Pincus to that characteristic of children.

Apparently unaware of the early work of Pohl-Pincus and Schein, M. Wharton Young recently reported some interesting studies concerning this problem in the course of which he came to essentially the same conclusions as did the two authors cited previously.[13] In his first paper, entitled "Anatomical Factors in Senile Alopecia; Experimental Production of Baldness," Young stated that "the constant pattern of senile alopecia suggests that there is a definite anatomical basis for this condition. Injection studies reveal a richer vascular supply in the marginal

12. (*a*) Young, M. W.: Anatomical Factors in Senile Alopecia: Experimental Production of Baldness, abstracted, Anat. Rec. **97**:378 (March) 1947; (*b*) Anatomical and Pathological Factors in Senile Alopecia, abstracted, ibid. **100**:728 (April) 1948.

13. Dr. Young supplied us with copies of the two papers which he presented at the 1947 and 1948 meetings of the American Association of Anatomists.

(muscular) zone of the scalp than in the central (aponeurotic) zone." Alopecia, as is well known, is confined to the central areas, whereas hair always persists in the marginal area overlying the occipital and auricular muscles. Further, Young stated that "the bald area shows a loss of hair follicles and fat with increased fibrosis in the subcutaneous layer." Finally, he summed up his experiments as follows: "Tension areas were produced experimentally in rhesus monkeys by suturing the free scalp edges after excising elliptical segments, thus reducing the circumference. These operations resulted in persistent baldness closely resembling the human types."

In his second paper, Young showed that scalp tension leads to reduction in the thickness of the soft tissues and interference with the circulation, with consequent loss of hair. He wrote, "X-ray studies of a series show that normally the soft tissue of the scalp is almost twice as thick as that over the bare forehead. This difference is apparently due to the greater amount of fat in the scalp and each globule is well vascularized. In the bald person, this differential is lost and the scalp thickness is reduced to that of the forehead, giving a thin halo over the cranium. All the bald heads showed this thinning by X-ray, and our autopsy cases showed loss of fat beneath the bald areas." Finally, he concluded that the cause of baldness is due to a disproportionate growth of the brain and of the skull in such a way that its external coverings cannot keep pace with it. He wrote, "Studies of adult growth show that in 'brainworkers,' where the circulation of the organ is enhanced, the brain continues to grow through the fifth decade or longer and many intellectuals are bald, but idiots and morons are seldom so. We believe that the differential adult growth leads to tension, to thinning, and to ischemia of the scalp with resulting loss of hair. Primitive man was not afflicted thus nor do women with their smaller brains suffer such a fate."

Comment: The two early papers by Schein state several factors which are operative in the production of baldness. Some of these appear to us as correct and others as erroneous. We believe the following points to be their outstanding contributions: 1. The role of tension of the scalp in the etiology of alopecia was suggested. 2. The specific distribution of alopecia was accounted for by local anatomic factors. 3. Histologic evidence of tissue changes in bald scalps, consisting of loss of subcutaneous fat and compression of tissue spaces, was presented.

Young's experiments demonstrated that tension of the scalp, surgically produced, leads to alopecia similar to that occurring in the human male. He also noted the loss of fat in the tissues of bald areas. Our disagreement with Young is over two chief points: 1. He referred to what we have designated ordinary human baldness as "senile alopecia." Actually, what he described and discussed is ordinary alopecia, which

characteristically has its onset in the twenties or thirties. It is not typically a condition of senility. 2. Young attributed the fact that women do not become bald to their having "smaller brains" and smaller heads. This view is untenable in the light of Hamilton's researches, referred to earlier.

A NEW INTEGRATED THEORY OF BALDNESS

As we noted in the introductory part of this paper, our interest in baldness was aroused by certain observations on facial expression in bald people. It was our impression, briefly, that many bald men, particularly those who started to lose their hair at an early age, have expressions suggestive of a pronounced and chronic tension of the facial muscles. In many, we encountered various types of "fixed smiles," and in a few, a rather striking, characteristic expression best described as a "toothy smile." Such rigid facial patterns are thought to reflect, psychologically speaking, defensive attitudes.

Wilhelm Reich in his book, "Character Analysis,"[14] pointed out what he called "muscular armor" as a frequently observed somatic reflection of "character armor." "Character armor" refers to the psychologic defenses of a neurotic personality which serve as protection from feelings of insecurity and anxiety. The sources of anxiety are felt to be external to the personality and are regarded as "attacks" on personal integrity. The somatic counterpart is a generalized tension of skeletal musculature as if the person were constantly alert to actual physical attack by others.

In animals the chief lifelong concern is biologic survival, whereas in man the chief importance has shifted to social survival (acceptance and success). Nevertheless, the basic feelings concerned have much in common, and many patterns of muscular innervation once significant when man functioned largely as an animal have been retained, though at present they are socially nonadaptive.

We have also stated that our observations lead us to some hypotheses concerning the role of scalp muscle activity in baldness. A review of the literature subsequently showed that there is considerable evidence in support of this idea. The next problem is the connection between facial expression and scalp muscle tension. In order to understand this relation clearly, it is necessary for one to consider the anatomy and particularly the evolutionary development and innervation of the epicranial muscles.[15] As is well known, the facial, or seventh cranial, nerve

14. Reich, W.: Character Analysis, ed. 2, New York, Orgone Institute Press, 1945.

15. (*a*) Huber, E.: Evolution of Facial Musculature and Facial Expression, Baltimore, Johns Hopkins Press, 1931. (*b*) Krieg, W. J. S.: Functional Neuroanatomy, Philadelphia, The Blakiston Company, 1942.

innervates the muscles of facial expression; however, it is perhaps less generally appreciated that branches of this same cranial nerve supply the muscles of the scalp and ears. As Young pointed out, "In the human embryo the scalp musculature is laid down as one continuous sheet covering the head and subsequently repeats its phyletic history of differentiation." [12b] This differentiation consists of gradual disappearance of muscle fibers from the middle portion of this sheet, i. e., roughly the top of the head, and they are replaced by fibrous tissue which is then called the galea aponeurotica. There thus remain two groups of muscle fibers, one over the forehead—the frontalis muscle—and the other over the occiput—the occipitalis muscle. It may be pointed out that only the occipitalis muscle has a bony insertion; the distal fibers of the frontalis blend in with the small facial muscles around the eyes and nose. This explains the fact that the predominant movement of the scalp is a backward one due to contraction of the occipitalis.

The posterior auricular branch of the facial nerve supplies both the posterior and the superior auricular muscles as well as the occipitalis. This fact accounts for the fact that movements of the ears, in man as well as in monkeys, are intimately associated with backward movements of the scalp.

Darwin, in his classic study "The Expression of the Emotions in Man and Animals," [16] pointed out that only animals that fight with their teeth have ability to draw back their ears. He expressed the belief that the purpose of this movement was primarily protective.[17] In its normal position, the ear presents a convenient hold for an attacking animal; however, when it is pulled back close to the head, this disadvantage to the attacked animal is minimal. In these animals, the ear movement due to contraction of the auricular muscles is accompanied by contraction of the occipitalis and usually by other preparations for fighting. Darwin concluded that many muscular correlates of feeling in men are (useless) vestiges of once meaningful behavior patterns. The human appendix represents the result of a somewhat analogous evolutionary process. It has been shown by others that tension of the scalp, by

16. Darwin, C.: The Expression of the Emotions in Man and Animals, New York, D. Appleton & Co., 1898.

17. He stated that "there can be hardly a doubt that the animals that fight with their teeth have acquired the habit of drawing back their ears closely to their heads, when feeling savage, from their progenitors having acted in this manner in order to protect their ears from being torn by their antagonists" (Darwin,[16] p. 353). We should like to add that it seems very likely that tightening of the scalp has the same significance, i. e., to prevent the attacking animal from gaining an advantageous purchase on the ordinarily loose skin of the head of the attacked animal.

producing chronic ischemia, may lead to alopecia. We feel that the tension is due to persistent activity of the scalp muscles—an outmoded physiologic concomitant of a basic defensive attitude.[18] We believe, therefore, that, in terms of biologic adaptation, baldness may be considered as an accidental end result of the phenomena described.

It should be noted that muscle tension cannot operate simply by compression of the soft tissues in which the blood vessels course; this is patently impossible, as the galea aponeurotica, which is put under tension by activity of the occipitalis muscle, lies *under* and not over the soft tissues of the scalp. Circulation is decreased, not by compression, but most probably by shearing stresses which pinch or kink the vessels. Such stresses, brought about by unequal displacements of the galea and dermis, may operate in one or both of two ways; either radially, i. e., by movement of the galea relative to overlying skin; or tangentially, i. e., by movement of the galea and overlying skin relative to laterally lying skin. The direction of the fibers of the two occipitalis muscles lie at an angle of about 20 degrees to each other. In addition, the galea is more adherent to the skull along the midline than laterally. These factors make for greater shear in the area on each side halfway between the midline and the lateral edge of the galea. It can be readily seen that the shape of the skull will have a great deal to do with the distribution of stresses and hence the exact pattern of interference of circulation and the resulting baldness. The mechanical problem involved is complex and warrants careful study.

Another important factor affecting the magnitude and effect of the shearing stress is the amount of fat in the subcutaneous tissue in which the blood vessels course. One of the general effects of testosterone is its influence on body fat. Not only does it produce an oilier skin and seborrhea in eunuchoid men, as Hamilton showed, but also it reduces the amount of subcutaneous fat. It is this fat padding of the scalp which, we believe, affords protection against baldness to women and prepubertal boys. Fat reduces the effect of shearing stress both by thickening the subcutaneous layer and by resisting deformation. Assuming that chronic muscular forces in the scalp are active in boys before puberty, in eunuchs and in women alike, we arrive at a theory which is able to account for all the clinical observations. It is only thus that we can understand why boys may begin to lose their hair soon after puberty; also, why some eunuchoid men become bald and others do not after

18. There is a certain analogy between this type of chronic muscle activity, finally leading to baldness, and other kinds of chronic muscle activity, which may lead to myositis and arthritis. (See Johnson, A.; Shapiro, L. B., and Alexander, F.: Preliminary Report on a Psychosomatic Study of Rheumatoid Arthritis, Psychosom. Med. **9**:295-300, 1947.)

treatment with male sex hormone, and why women, who ordinarily do not have this kind of alopecia, may acquire it rapidly under the influence of masculinizing tumors and gradually with old age and its slow masculin-

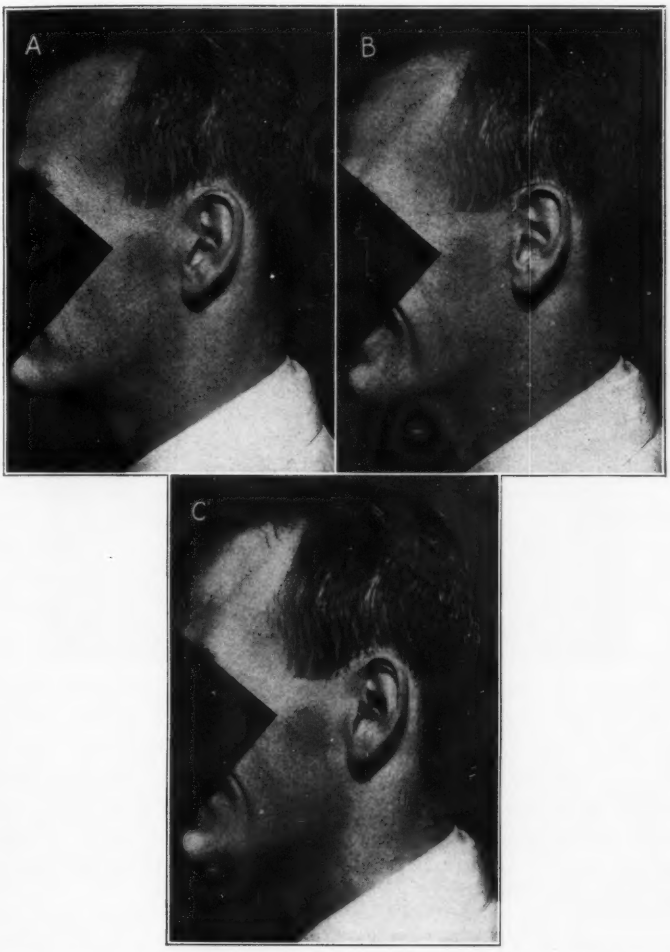

Fig. 1.—*A*, a photograph of the face at rest. *B*, a photograph taken in exactly the same position as *A*, with the subject smiling. *C*, a composite picture, made from a contact print made from the superimposed negatives of *A* and *B*.

izing changes. That hereditary factors play a role in this condition is strongly suggested by all the evidence available. The theory which we have proposed is essentially independent of such considerations. Genetic

factors may be operative by determining the shape of the head, as suggested by Schein, or possibly by predisposing to certain more archaic kinds of muscular expression.

The accompanying photographs illustrate the scalp and ear movements implicated in the production of baldness. Figure 1 *A* is the picture of the face at rest; figure 1 *B* was taken in exactly the same position, with the subject smiling. Figure 1 *C* is a composite picture, from a contact print made from the exactly superimposed negatives of figures 1 *A* and *B*. Figure 2 is an enlargement of the view of the frontoparietal region shown in figure 1 *C*.

Figure 1 *A* and *B* shows most clearly the upward displacement of the ear which accompanied smiling. The presence of the crease above the ear in the first photograph indicates the relative chronicity of tension in

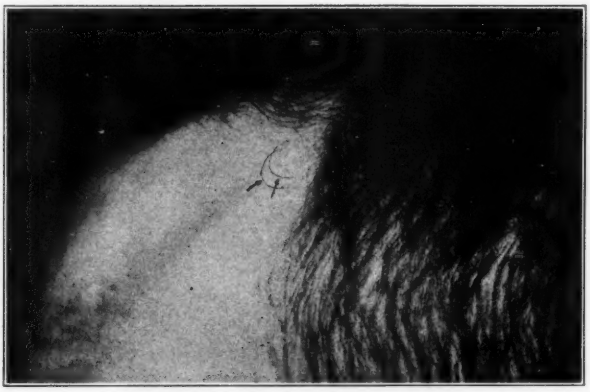

Fig. 2.—An enlargement of the view of the frontoparietal region shown in figure 1 *C*.

this area. The composite picture reveals the movement of the scalp otherwise not discernible in the two pictures. This is seen most readily in the enlargement (retouched) by the double images of individual hairs in the frontoparietal region (as indicated by the arrows). It seems that the amount of displacement of the skin is roughly proportional to the degree of baldness.

ELECTROMYOGRAPHIC STUDIES

In line with these theoretic concepts concerning scalp muscle activity in baldness, we undertook an electromyographic study of a number of bald and nonbald subjects in an attempt to determine whether significant differences in scalp muscle activity were demonstrable between two such groups. The following remarks comprise a brief résumé of the experiments.

The study consisted of recording scalp electromyograms. The apparatus used consisted of an ordinary multiple channel electroencephalograph.[19] One pair of electrodes was placed at the vertex on either side of the midline and the other pair close together over the belly of the left occipitalis muscle. Electrical activity emanating from essentially one source (occipitalis) was thus recorded from two different areas. Muscle activity was found to have much greater amplitude than brain waves, and in addition there were such pronounced differences in wave form that the two could be distinguished without difficulty.

The subjects were medical students and colleagues, all less than 40 years of age. Most of the bald persons reported that they had first noted thinning of the hair in their early twenties.

At the beginning of the experiments, we expected to find that the bald subjects would show continuous or near-continuous activity of the occipitalis muscle under all conditions. This was not found to be the case. All bald and nonbald subjects were able, while lying prone, to relax so that the scalp showed no detectable muscle potential. There were no consistent differences in the time required to bring about relaxation of the scalp muscles in the two groups.

Laughing, smiling, biting and voluntary movements of the ear (in those who could make them) were accompanied by definite and correlated electrical discharges from the scalp in all persons studied.

A total of 27 records on 21 persons was obtained. Seventeen records (13 men) were of bald persons, and 10 records (8 men and 2 women) were of nonbald persons. Maximum voltages in the electromyograms were measured while the subjects were laughing, smiling, biting and, in some cases, wiggling the ears. As a rule, higher voltage activity was recorded from the occipital electrodes than from those placed at the vertex, except in connection with biting. The maximum voltage observed, slightly over 1 volt, occurred during ear wiggling in a nonbald subject. No consistent and significant differences between bald and nonbald subjects were demonstrable with these methods.

The technic outlined was based on an attempt to establish a correlation between the intensity of scalp contraction in response to the various stimuli and the loss or retention of hair. It was impossible for us to standardize the stimulus for laughter and smiling, because of obvious individual differences in responsiveness and also because of variations from time to time within the same persons. There are too many uncontrolled variables in this experiment, and also the situation is a very artificial one. We believe, however, that the chief reason for our failure to detect significant differences in scalp muscle activity in bald and non-

19. Dr. Theodore J. Case, Associate Professor of Neurophysiology at the University of Chicago, gave us permission to use the facilities of the electroencephalographic laboratory. Miss Ann Falknor provided technical assistance.

bald subjects was the acute character of these experiments. According to our theory of baldness, the process which leads to tension over the vertex of the head must be a slowly acting and chronic one.

SOME SUGGESTIONS FOR FURTHER EXPERIMENTAL WORK

Unfortunately, we were not in a position to undertake any but the simplest kind of experimental procedures in an attempt to verify this theory. The electromyographic studies led to inconclusive results. However, since a number of possible experimental studies have suggested themselves to us, a brief outline of these is included in the hope of stimulating further research.

1. *Electrical Stimulation.*—This might be tried with branches of the seventh cranial nerve supplying the occipitalis muscles in monkeys. Since the changes which lead to baldness in human beings are characteristically of a chronic kind, it is desirable for one to reproduce similar conditions in experiments.

2. *Measurrements of Circulation in the Scalp.*—Recent technics employing radioactive indicators injected into the blood stream might advantageously be utilized to demonstrate decreased blood flow in areas which show beginning loss of hair. Men who can readily contract their scalps voluntarily could also be used in experiments and the circulation measured during contraction and relaxation.

3. *Electromyographic Studies.*—Those carried out by us consisted of tracings recorded over a relatively brief period of time, usually not over thirty minutes. It may well be that records taken over longer periods of time would reveal significant differences between bald and nonbald groups. However, the recording of scalp muscle activity during the night might be the most promising method of using this particular technic.[20]

4. *Psychoanalysis.*—Psychoanalytic study of young men who are becoming bald might contribute to our understanding of the emotional factors leading to scalp muscle tension. The possibility of a relation between the etiology of certain types of headaches [21] and baldness should be considered. We have no personal observations on the specific

20. An analogy may be found in the use of studies on nocturnal gastric secretion in patients with duodenal ulcers (Dragstedt, L. R.: Section of the Vagus Nerves to the Stomach in the Treatment of Peptic Ulcer, Surg., Gynec. & Obst. **83**:547-549 [Oct.] 1946. Levin, E.; Kirsner, J. B.; Palmer, W. L., and Butler, C.: Nocturnal Gastric Secretion: Studies on Normal Subjects and on Patients with Duodenal Ulcer, Gastric Ulcer and Gastric Carcinoma, Arch. Surg. **56**: 345-356 [March] 1948).

21. Simons, D. J., and Wolff, H. G.: Studies on Headache: Mechanism of Chronic Post-Traumatic Headache, Psychosom. Med. **8**:227-242, 1946.

emotional situations, if any, which may lead to this type of innervation. It may be noted, however, that forceful and derisive laughter often results in feelings of tension and ache in the occipital region.

THERAPEUTIC IMPLICATIONS

According to the theory presented, ordinary human baldness is the result of chronic hyperactivity of the scalp muscles. It follows from this view that any interruption of the nervous stimuli to the muscles involved, if performed before irreversible local changes have occurred, would serve to arrest the process and possibly lead to regrowth of hair in areas only partially damaged. Practically, injection of procaine or alcohol into the branches of the facial nerves innervating the occipitalis muscles might achieve the desired result temporarily; bilateral section would provide a more permanent and complete type of severance. Only those branches of the facial nerves which innervate the occipitalis muscles need be sectioned; this should be a relatively simple and harmless procedure.

Admittedly, the therapeutic implications of this theory are, at the present time, only speculative. Actual clinical trial of the procedure not only would serve to establish its possible therapeutic and prophylactic value but also would, if successful, constitute experimental evidence for the validity of the theory presented.

SUMMARY

Observations on the facial expressions of bald persons stimulated some hypotheses concerning the role of tension of the scalp muscles in the etiology of ordinary human alopecia.

A brief critical review of the literature was presented. The various hypotheses which have been advanced were discussed under the following headings: (1) seborrhea, (2) hormones, (3) tightly fitting hats, (4) heredity and (5) tension of the scalp.

Our theory is based on some early observations of Darwin's on the defensive significance of retraction of the ears in animals that fight with their teeth. It was shown that there is an intimate association, both from the point of view of embryologic development and innervation, between the muscles of the face, ears and scalp. The explanation was advanced that ordinary alopecia is the end result of chronic activity of the scalp muscles (via branches of the facial nerves) which leads to shearing stresses in the dermis of the scalp and consequent ischemia. The specific pattern of baldness is accounted for by the anatomy and mechanics of the structures involved.

In man's phylogenetic past, this pattern of muscular contraction served a defensive purpose. Now, though biologically nonadaptive, it persists in some persons as an expression of defensive attitudes. The

role of the male sex hormone in baldness is related to its effect on the distribution of body fat. Women and children have a thicker subcutaneous fat padding in the scalp, which resists the blood vessel–pinching effect of shearing stresses. Testosterone, in reducing the thickness of this cushion, is thus one of the prerequisites for the development of ordinary alopecia. Genetic factors probably act by predisposing to certain skull shapes which favor the development of great tension of the scalp or possibly by determining affinities for more archaic kinds of muscular expression.

Electromyographic studies were undertaken in an attempt to provide evidence for this thesis. The results, based on experiments of an essentially acute character, did not reveal significant differences between the scalp muscle activity of bald and of nonbald persons. Certain suggestions for further experimental work were presented.

It follows from our theory that interruption of chronic scalp muscle activity will be of prophylactic and therapeutic value. We suggest that bilateral section of the branches of the facial nerve supplying the occipitalis muscles be tried in early cases.

ADDENDUM.—Since this paper was submitted for publication, there appeared an article by Light [22] on histologic studies of human scalps which "were obtained during autopsy shortly after death due to unnatural causes including many types of accidents and homicide." Light found that with increasing age there was (1) a tendency toward a decrease in the number of hairs in the crown area (of males) and (2) an increase of connective tissue infiltration into the fat layer of the skin in the same areas. He stated that "there is a definite trend to lack of hair when the connective tissue infiltrates the fat layer and decreases its volume in the region where the hair root grows." Light concluded the article with the speculation that "If it is assumed that in restricted areas certain unusual physiological processes are at work for a time before actual baldness is evident, the measurement of these processes would be very helpful in predicting baldness and might lead to preventive measures." We believe that the chronic and persistent activity of the scalp muscles, leading to compression and anoxia of the subcutaneous tissues in areas overlying the galea aponeurotica, as described in our paper, constitutes the "unusual physiological processes" postulated by Light.

737 North Michigan Avenue.

950 East Fifty-Ninth Street.

22. Light, A. M.: Histological Study of Human Scalps Exhibiting Various Degrees of Non-Specific Baldness, J. Invest. Dermat. **13**:53-59 (Aug.) 1949.

PENICILLIN IN THE TREATMENT OF EXPERIMENTAL SYPHILIS OF RABBITS

V. The Synergistic or Additive Activity of Penicillin Injected Intramuscularly with Sodium Iodide Administered Orally and Intravenously

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With the Technical Assistance of ANNA M. RULE
PHILADELPHIA

ALTHOUGH the iodides have been employed in the treatment of syphilis since 1821, their mode of action has been obscure. Clinical experience has shown that they have little or no therapeutic effect in the early stages of the disease, this fact being due, it is commonly stated, to the absence of spirocheticidal activity. Thus Tomasczewski [1] in 1910 reported that potassium iodide had no prophylactic or curative activity in the treatment of experimental syphilis of monkeys and rabbits. Nichols [2] also reported that single intravenous injections of potassium iodide in doses of 0.01 and 0.03 Gm. per kilogram of body weight were ineffective in the treatment of 3 rabbits with acute testicular syphilis, although the intramuscular injection of 1 Gm. per kilogram into a fourth animal resulted in evidences of spirocheticidal activity. At the same time, however, Neisser [3] reported that it was possible to prevent the development of primary lesions in monkeys by treatment with potassium iodide, if massive doses of from 7 to 8 Gm. were administered subcutaneously at the time of or four days after inoculation. He did not state, however, whether or not secondary lesions ultimately developed. Furthermore, the results of his reinoculation and tissue inoculation experiments designed to demonstrate the presence or absence of Treponema pallidum were inconsistent.

Pearce [4] subsequently reported that eighteen to nineteen intravenous injections of potassium iodide in doses of 0.0003 or 0.006 Gm. per kilo-

From the Research Institute of Cutaneous Medicine.

1. Tomasczewski: Untersuchungen über die Wirkungen des Quecksilbers und Jods bei der experimentallen Syphilis, Deutsche med. Wchnschr. **36**:653 (April) 1910.

2. Nichols, H. J.: Further Observations on Certain Features of Experimental Syphilis and Yaws in the Rabbit, J. Exper. Med. **14**:196 (Aug.) 1911.

3. Neisser, A.: Erforschung der Syphilis, Arb. a.d.k. Gsndhtsamte **30**:261, 1910.

4. Pearce, L.: Therapeutic Action of Potassium Iodid in Experimental Syphilis of the Rabbit, Arch. Dermat. & Syph. **12**:1 (July) 1925.

gram at biweekly or weekly intervals into syphilitic rabbits resulted in modifying the severity and in shortening the duration of the experimental disease as measured by the character both of the primary orchitis and of the general manifestations. Since the disease which developed in the rabbits treated with iodide resembled that of untreated animals of relatively high resistance in which few or no secondary lesions developed, Pearce suggested that the therapeutic activity of potassium iodide in experimental syphilis of rabbits may be due to a stimulation or a reenforcement of the host's mechanism of reaction or defense.

In the experiments of one of us (J. A. K.) with Harkins [5] it was found that the intravenous injection of sodium and potassium iodides into rabbits with acute syphilitic orchitis, in doses of 0.060 and 0.030 Gm. per kilogram, respectively, once a day for ten days in succession, resulted in evidences of spirocheticidal activity in the way of promotion of healing and negative results on dark field examinations for T. pallidum; complete or biologic cures, however, were not observed, since positive results occurred on transfer of lymph nodes. Similar results were observed when sodium and potassium iodides were administered orally in doses of 0.120 and 0.100 Gm. per kilogram, respectively, once a day for ten days in succession.

Under the circumstances there can be no denial of the fact that potassium and sodium iodides possess a slight degree of spirocheticidal activity. It is assumed that their therapeutic efficacy in the treatment of late or chronic acquired and congenital syphilis, however, is largely based on their bringing about the resolution or absorption of gummatous lesions and syphilitic exudates by their ability to neutralize antienzymes, as suggested by Jobling and Petersen,[6] which activity in itself is of therapeutic benefit aside from the fact that it may open the way for the action of more spirocheticidal agents administered at the same time.

Furthermore, the results of the experiments of one of us (J. A. K.), conducted about twenty-four years ago, have shown that the iodides apparently act synergistically or additively to some degree with arsphenamine injected intravenously, mercuric salicylate injected intramuscularly and mercurial ointment administered by inunction in the treatment of chronic experimental syphilis of rabbits.[7] And since it is now well established that penicillin has pronounced synergistic activity when administered conjointly with oxophenarsine hydrochloride

5. Kolmer, J. A.: Principles and Practice of Chemotherapy with Special Reference to the Specific and General Treatment of Syphilis, Philadelphia, W. B. Saunders Company, 1926, p. 337.

6. Jobling, J. W., and Petersen, W.: The Therapeutic Action of Iodin, Arch. Int. Med. **15**:286 (Feb.) 1915.

7. Footnote 5, p. 351.

(mapharsen®)[8] and with bismuth compounds[9] in the treatment of experimental syphilis of rabbits, the purpose of this investigation was not only to restudy the spirocheticidal activity of iodides alone, but especially to determine whether or not these compounds act synergistically or additively with penicillin in the treatment of the disease.

METHODS AND MATERIALS

In our experiments all rabbits were inoculated intratesticularly with the Nichols-Hough strain of T. pallidum. Acute orchitis developed in all, with strongly positive results on dark field examinations about five or six weeks thereafter, when treatment was instituted. Dark field examinations were then made once a day for three days in succession and thereafter once a week over a total period of seventy days. At the expiration of that time the popliteal lymph nodes of all treated animals were inoculated into the testicles of fresh animals, which were kept under observation for a minimum of four months, when the results were evaluated.

The penicillin employed was commercial crystalline G. Solutions were freshly prepared with sterile isotonic solutions of sodium chloride and administered by intramuscular injection twice daily (10 a.m. and 3 p.m.) for eight days in succession.

Sodium iodide was employed because of being less toxic than potassium iodide by intravenous injection. Solutions were prepared in sterile distilled water and administered intravenously or orally by stomach tube twice daily (10 a.m. and 3 p.m.) for eight days in succession.

RESULTS OBSERVED

Multiple Doses of Penicillin in Isotonic Solution of Sodium Chloride Injected Intramuscularly.—As shown in table 1, the minimal curative dose of penicillin administered intramuscularly twice daily for eight days in succession was approximately 500 units per dose or a total of 8,000 units per kilogram of body weight. This observation corresponds closely to the results previously reported, in which the curative dose was less than 1,000 units per kilogram when given twice daily for eight days in succession.[10]

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8. (*a*) Eagle, H.; Magnuson, H. J., and Fleischman, R.: The Synergistic Action of Penicillin and Mapharsen (Oxophenarsine Hydrochloride) in the Treatment of Experimental Syphilis, J. Ven. Dis. Inform. **27**:3 (Jan.) 1946. (*b*) Kolmer, J. A., and Rule, A. M.: Penicillin in the Treatment of Experimental Syphilis of Rabbits: II. The Synergistic or Additive Activity of Penicillin, Oxophenarsine Hydrochloride and Bismuth and Potassium Tartrate, Arch. Dermat. & Syph. **56**:179 (Aug.) 1947.

9. Kolmer and Rule[8b]; The Synergistic or Additive Activity of Chemotherapeutic Compounds, Am. J. M. Sc. **215**:136 (Feb.) 1948.

10. Kolmer, J. A., and Rule, A. M.: Penicillin in the Treatment of Experimental Syphilis of Rabbits: I. The Therapeutic Activity of Penicillin in Single and Multiple Doses in Isotonic Solution of Sodium Chloride and Peanut Oil-Beeswax by Intramuscular Injection, Arch. Dermat. & Syph. **55**:741 (June) 1947.

Multiple Doses of Sodium Iodide in Aqueous Solution Administered Orally and by Intravenous Injection.—Since the maximum single tolerated dose of sodium iodide for rabbits when given by intravenous injection is about 2.5 Gm. per kilogram, while that of potassium iodide is about 0.310 Gm. per kilogram, sodium iodide was chosen because of being about eight times less toxic for rabbits than the potassium salt by this route of administration.[5] Rabbits given two intravenous injections per day for eight days in succession in doses of 0.025, 0.050 and 0.100 Gm. per kilogram, totaling 0.4 to 1.6 Gm. per kilogram, showed no evidences of toxicity. The same was true for animals given two doses of 0.050, 0.100 and 0.150 Gm. per kilogram orally (by stomach tube) per day for eight days in succession, for a total of 0.8 to 2.4 Gm. per kilogram.

TABLE 1.—*Multiple Intramuscular Injections of Penicillin in Isotonic Solution of Sodium Chloride in the Treatment of Acute Syphilitic Orchitis of Rabbits*

No.	Dose, Units per Kg.*	Total Dose, Units per Kg.	Results of Dark Field Examinations for T. Pallidum, Days †												Results of Transfer of Lymph Nodes
			1	2	3	7	14	21	28	35	42	49	56	63	70	
1	100	1,600	4	4	4	3	1	—	—	—	—	4	4	4	4	Positive
2	100	1,600	4	4	4	4	—	—	—	—	—	2	4	4	4	Positive
3	250	4,000	4	4	4	2	—	—	—	—	—	2	4	4	4	Positive
4	250	4,000	4	4	3	1	—	—	—	—	—	—	4	4	4	Positive
5	500	8,000	4	4	4	—	—	—	—	—	—	—	—	—	—	Negative
6	500	8,000	4	4	4	—	—	—	—	—	—	—	—	—	—	Negative
7	1,000	16,000	4	4	3	—	—	—	—	—	—	—	—	—	—	Negative
8	1,000	16,000	4	4	2	—	—	—	—	—	—	—	—	—	—	Negative

* Administered twice daily for eight days in succession.
† After institution of treatment: 4 indicates large numbers of actively motile spirochetes per dark field; 3, 2 and 1 indicate smaller numbers of spirochetes per dark field, respectively; — indicates negative results on dark field examinations.

As shown in table 2, a total dose of 0.8 to 1.6 Gm. per kilogram injected intravenously and a total dose of 1.6 to 2.4 Gm. per kilogram administered orally apparently showed a slight degree of spirocheticidal activity on the basis of the results of dark field examinations, but none of the animals showed complete or biologic cure since transfers of lymph nodes of all treated animals gave positive results.

Synergistic or Additive Activity of Multiple Doses of Penicillin Injected Intramuscularly and Multiple Doses of Sodium Iodide Administered Orally.—While two intramuscular injections of penicillin in doses of 250 units per kilogram per day for eight days in succession, for a total of 4,000 units per kilogram, were not completely curative (table 1), yet this dose was completely curative when administered along with two doses of 0.100 Gm. of sodium iodide given orally per day for eight days in succession, as shown in table 3. In other words, while this dose of sodium iodide alone was not curative (table 2), yet it appeared to act

synergistically or additively when administered along with approximately one-half the minimal curative dose of penicillin administered twice daily by intramuscular injection for eight days in succession.

TABLE 2.—*Multiple Doses of Sodium Iodide Administered in Aqueous Solution Orally and Intravenously in the Treatment of Acute Syphilitic Orchitis of Rabbits*

	Orally		Intravenously		Results of Dark Field Examinations for T. Pallidum, Days †													Results of Transfer of Lymph Nodes
No.	Dose, Gm. per Kg.*	Total Dose, Gm. per Kg.	Dose, Gm. per Kg.	Total Dose, Gm. per Kg.	1	2	3	7	14	21	28	35	42	49	56	63	70	
1	0.050	0.800	.....	...	4	4	4	4	2	—	—	—	—	4	4	4	4	Positive
2	0.050	0.800	.....	...	4	4	4	4	1	—	—	—	—	2	4	4	4	Positive
3	0.100	1.6	.....	...	4	4	4	2	—	—	—	—	—	—	4	4	4	Positive
4	0.100	1.6	.....	...	4	4	4	3	—	—	—	—	—	2	4	4	4	Positive
5	0.150	2.4	.....	...	4	4	4	2	—	—	—	—	—	—	4	4	4	Positive
6	0.150	2.4	.....	...	4	4	4	2	—	—	—	—	—	—	2	4	4	Positive
7	.....	...	0.025	0.4	4	4	4	3	2	—	—	—	—	2	4	4	4	Positive
8	.....	...	0.025	0.4	4	4	4	3	1	—	—	—	—	4	4	4	4	Positive
9	.....	...	0.050	0.8	4	4	4	3	—	—	—	—	2	4	4	4	4	Positive
10	.....	...	0.050	0.8	4	4	4	2	—	—	—	—	—	—	4	4	4	Positive
11	.....	...	0.100	1.6	4	4	3	1	—	—	—	—	4	4	4	4	4	Positive
12	.....	...	0.100	1.6	4	4	3	—	—	—	—	—	—	2	4	4	4	Positive

* Administered twice daily for eight days in succession.
† After institution of treatment: 4 indicates large numbers of actively motile spirochetes per dark field; 3, 2 and 1 indicate smaller numbers of spirochetes per dark field, respectively; — indicates negative results on dark field examinations.

TABLE 3.—*The Synergistic Activity of Multiple Intramuscular Injections of Penicillin in Isotonic Solution of Sodium Chloride and Multiple Doses of Sodium Iodide in Aqueous Solution Administered Orally*

	Penicillin *		Sodium Iodide †		Results of Dark Field Examinations for T. Pallidum, Days ‡													Results of Transfer of Lymph Nodes
No.	Units per Kg.	Total	Gm. per Kg.	Total	1	2	3	7	14	21	28	35	42	49	56	63	70	
1	100	1,600	0.100	1.6	4	4	4	3	—	—	—	—	—	—	2	4	4	Positive
2	100	1,600	0.100	1.6	4	4	4	2	—	—	—	—	—	—	—	4	4	Positive
3	250	4,000	0.100	1.6	4	4	4	—	—	—	—	—	—	—	—	—	—	Negative
4	250	4,000	0.100	1.6	4	4	4	—	—	—	—	—	—	—	—	—	—	Negative
5	500	8,000	0.100	1.6	4	4	2	—	—	—	—	—	—	—	—	—	—	Negative
6	500	8,000	0.100	1.6	4	4	1	—	—	—	—	—	—	—	—	—	—	Negative
7	1,000	16,000	0.100	1.6	4	4	1	—	—	—	—	—	—	—	—	—	—	Negative
8	1,000	16,000	0.100	1.6	4	4	2	—	—	—	—	—	—	—	—	—	—	Negative

* Given twice daily by intramuscular injection for eight days in succession.
† Given twice daily by oral administration for eight days in succession.
‡ After institution of treatment: 4 indicates large numbers of actively motile spirochetes per dark field; 3, 2 and 1 indicate smaller numbers of spirochetes per dark field, respectively; — indicates negative results on dark field examinations.

Synergistic or Additive Activity of Multiple Intramuscular Injections of Penicillin and Multiple Intravenous Injections of Sodium Iodide.—Exactly similar results were observed when sodium iodide was administered by intravenous injection, as shown in table 4. Possibly

sodium iodide alone is somewhat more spirocheticidal by this route of administration than by oral administration (table 3), but the differences observed on the basis of dark field examinations could well be within the range of experimental error. Certainly it appears that the synergistic or additive effects of sodium iodide administered orally on penicillin are practically the same as those seen when the sodium iodide is injected intravenously. At all events, though a dose of penicillin of 250 units per kilogram twice daily for eight days in succession is only about one-half the minimal curative dose, when it is administered along with 0.1 Gm. of sodium iodide injected intravenously twice daily for eight days in succession, well defined synergistic or additive effects are observed.

TABLE 4.—*The Synergistic Activity of Multiple Intramuscular Injections of Penicillin in Isotonic Solution of Sodium Chloride and Multiple Intravenous Injections of Sodium Iodide in Aqueous Solution*

	Penicillin *		Sodium Iodide †		Results of Dark Field Examinations for T. Pallidum, Days ‡													Results of Transfer of Lymph Nodes
No.	Units per Kg.	Total	Gm. per Kg.	Total	1	2	3	7	14	21	28	35	42	49	56	63	70	
1	100	1,600	0.100	1.6	4	4	2	—	—	—	—	—	—	—	1	4	4	Positive
2	100	1,600	0.100	1.6	4	4	4	—	—	—	—	—	—	—	3	4	4	Positive
3	250	4,000	0.100	1.6	4	4	2	—	—	—	—	—	—	—	—	—	—	Negative
4	250	4,000	0.100	1.6	4	4	2	—	—	—	—	—	—	—	—	—	—	Negative
5	500	8,000	0.100	1.6	4	4	1	—	—	—	—	—	—	—	—	—	—	Negative
6	500	8,000	0.100	1.6	4	4	2	—	—	—	—	—	—	—	—	—	—	Negative
7	1,000	16,000	0.100	1.6	4	4	1	—	—	—	—	—	—	—	—	—	—	Negative
8	1,000	16,000	0.100	1.6	4	4	1	—	—	—	—	—	—	—	—	—	—	Negative

* Given twice daily by intramuscular injection for eight days in succession.
† Given twice daily by intravenous injection for eight days in succession.
‡ After institution of treatment: 4 indicates large numbers of actively motile spirochetes per dark field; 3, 2 and 1 indicate smaller numbers of spirochetes per dark field, respectively; — indicates negative results on dark field examinations.

COMMENTS

Under the circumstances it appears that sodium iodide alone, and presumably potassium iodide as well, administered orally and intravenously may be slightly spirocheticidal in the treatment of rabbits with acute syphilitic orchitis. Be this as it may, however, it appears that an iodide administered orally or by intravenous injection has a definite synergistic or additive spirocheticidal effect when given along with intramuscular injections of penicillin in the treatment of this disease.

Consequently, though there appears to be no justification for using an iodide and penicillin conjointly in the treatment of early syphilis, I believe that there is a substantial experimental basis for such combined, synergistic or additive chemotherapy in the therapeutic management of late acquired and congenital syphilis. Surprisingly enough, it appears that this synergistic or additive activity of penicillin and an iodide may

be more pronounced than that of the organic arsenicals or mercury and an iodide, although this opinion is based only on the results observed by one of us (J. A. K.) about twenty-four years ago, as previously discussed.

To the best of our knowledge the conjoint oral administration of potassium or sodium iodide along with intramuscular injection of penicillin has not been advocated in the treatment of late or chronic acquired and congenital syphilis, although one of us (J. A. K.) has always administered potassium iodide orally three times a day, before meals, in the penicillin therapy of patients with both acquired and congenital chronic or late cases of the disease. Needless to state, it is difficult to appraise the therapeutic effects of penicillin alone versus those of penicillin and iodide conjointly in treatment, but I believe that an iodide should always be administered at the same time as the penicillin. As a matter of fact, it is the custom of one of us (J. A. K.) to start the administration of potassium iodide orally in the maximum tolerated dose three times a day, before meals, about four weeks before starting the administration of penicillin in order to obtain the resolving effects of the iodide on microscopic and macroscopic gummatous lesions before the administration of the latter compound is begun, while the oral administration of the iodide is continued throughout the course of penicillin therapy.

SUMMARY

The approximate minimal curative dose of penicillin given by intramuscular injection twice daily for eight days in succession, in the treatment of acute syphilitic orchitis of rabbits, was 500 units per kilogram per dose, for a total of about 8,000 units.

Sodium iodide in a dose of 0.025 to 0.100 Gm. per kilogram by intravenous injection twice daily for eight days in succession, for a total of 0.4 to 1.6 Gm. per kilogram, was slightly spirocheticidal but not completely curative in the treatment of acute syphilitic orchitis of rabbits. The same observation was true for sodium iodide in a dose of 0.050 to 0.150 Gm. given orally twice daily for eight days in succession, for a total of 0.8 to 2.4 Gm. per kilogram.

However, the intramuscular injection of 250 units of penicillin per kilogram twice daily for eight days in succession, for a total of 4,000 units per kilogram, along with the oral or intravenous administration of sodium iodide twice daily for eight days in succession in doses of 0.1 Gm. per kilogram for a total of 1.6 Gm. per kilogram, was completely curative in the treatment of acute syphilitic orchitis of rabbits.

Under the circumstances it appears that penicillin and iodides act synergistically or additively in the treatment of experimental syphilis.

The advisability of administering iodides conjointly with penicillin in the treatment of late acquired and congenital syphilis is discussed.

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PENICILLIN IN THE TREATMENT OF EXPERIMENTAL SYPHILIS OF RABBITS

VI. The Synergistic or Additive Activity of Penicillin Injected Intramuscularly and Tryparsamide Administered Intravenously

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With the Technical Assistance of ANNA M. RULE

PHILADELPHIA

IN 1919 Brown and Pearce [1] reported that tryparsamide, the sodium salt of *p*-N-phenylglycineamidoarsonic acid, was effective in the treatment of experimental syphilis of rabbits when administered by intravenous injection in single doses of 0.4 to 0.5 Gm. per kilogram of body weight. This statement was based on the observation of negative results on dark field examinations for Treponema pallidum after the administration of the compound, along with healing of the testicular lesions and the absence of recurrent infections, although transfers of lymph nodes to fresh animals as a test for complete or biologic cure were not conducted. The maximal single tolerated dose for rabbits by intravenous injection was from 0.75 and 1.0 Gm. per kilogram,[2] so that the chemotherapeutic index of tryparsamide has been stated to be about 2. The results of our experiments, reported herewith, have shown that the maximal single tolerated dose for rabbits by intravenous injection is about 0.9 Gm. per kilogram, with a minimal single curative dose of about 0.6 Gm. per kilogram, the chemotherapeutic index thus being about 1.5.

Under the circumstances tryparsamide has been regarded as being too low in spirocheticidal activity for the treatment of early syphilis. But because the compound possesses some degree of spirocheticidal activity and a high degree of penetrability for the tissues of the central nervous system, it has been employed in treatment in selected cases of late syphilis of the brain, spinal cord and meninges without optic atrophy or neuroretinitis. Consequently, we have thought it advisable to deter-

From the Research Institute of Cutaneous Medicine.

1. Brown, W. H., and Pearce, L.: Chemotherapy of Trypanosome and Spirochete Infections: IV. The Action of N-Phenylglycineamide-*p*-Arsonic Acid upon Spirochete Infections, J. Exper. Med. **30**:483 (Nov.) 1919.

2. Brown, W. H., and Pearce, L.: Chemotherapy of Trypanosome and Spirochete Infections: I. The Toxic Action of N-Phenylglycineamide-*p*-Arsonic Acid, J. Exper. Med. **30**:417 (Nov.) 1919.

mine whether or not the combined treatment of acute syphilitic orchitis of rabbits with penicillin and tryparsamide produces any evidences of synergistic or additive spirocheticidal activity.

METHODS AND MATERIALS

In our experiments all rabbits were inoculated intratesticularly with the Nichols-Hough strain of T. pallidum. Acute orchitis developed in all, with strongly positive results on dark field examinations about five or six weeks thereafter, when treatment was instituted. Dark field examinations were then made once a day for three days in succession and thereafter once a week, over a total period of seventy days. At the expiration of that time the popliteal lymph nodes of all treated animals were inoculated into the testicles of fresh animals, which were kept under observation for a minimum of four months, when the results were evaluated.

The penicillin employed was commercial crystalline G. Solutions were freshly prepared with sterile isotonic solutions of sodium chloride and administered by

TABLE 1.—*Single Intramuscular Injections of Penicillin in Isotonic Solution of Sodium Chloride in the Treatment of Acute Syphilitic Orchitis of Rabbits*

No.	Units per Kg.	Results of Dark Field Examinations for T. Pallidum, Days *												Results of Transfer of Lymph Nodes
		1	2	3	7	14	21	28	35	42	49	56	63	70	
1	25,000	1	1	—	—	2	4	4	4	4	4	4	4	4	Positive
2	25,000	1	1	—	—	4	4	4	4	4	4	4	4	4	Positive
3	50,000	1	—	—	—	4	4	4	4	4	4	4	4	4	Positive
4	50,000	1	—	—	—	2	4	4	4	4	4	4	4	4	Positive
5	100,000	1	—	—	—	—	—	—	—	—	—	—	—	—	Positive
6	100,000	1	—	—	—	—	—	—	—	—	—	—	—	—	Positive
7	200,000	—	—	—	—	—	—	—	—	—	—	—	—	—	Negative
8	200,000	—	—	—	—	—	—	—	—	—	—	—	—	—	Negative
9	300,000	—	—	—	—	—	—	—	—	—	—	—	—	—	Negative
10	300,000	—	—	—	—	—	—	—	—	—	—	—	—	—	Negative

* After institution of treatment: 4 indicates large numbers of actively motile spirochetes per dark field; 3, 2 and 1 indicate smaller numbers of spirochetes per dark field, respectively; — indicates negative results on dark field examinations.

intramuscular injection. Solutions of tryparsamide were freshly prepared in sterile distilled water and administered intravenously.

RESULTS OBSERVED

Single Intramuscular Injections of Penicillin.—As previously reported,[3] we have found that the single minimal curative dose of commercial penicillin in an isotonic solution of sodium chloride, injected intramuscularly, was more than 100,000 units per kilogram of body weight in the treatment of acute syphilitic orchitis of rabbits. In these experiments the dose was found to be approximately 200,000 units per kilogram of body weight (table 1).

3. Kolmer, J. A., and Rule, A. M.: Penicillin in the Treatment of Experimental Syphilis of Rabbits: I. The Therapeutic Activity of Penicillin in Single and Multiple Doses in Isotonic Solution of Sodium Chloride and Peanut Oil-Beeswax by Intramuscular Injection, Arch. Dermat. & Syph. **55**:741 (June) 1947.

Single Intravenous Injections of Tryparsamide.—As shown in table 2, the single minimal curative dose of tryparsamide injected intravenously was found to be about 0.6 Gm. per kilogram of weight, since 1 of 2 rabbits showed complete or biologic cure after the administration of this dose, while both of 2 rabbits given 0.8 Gm. per kilogram showed complete or biologic cure. Two animals given 1.0 Gm. per kilogram, however, succumbed to the toxicity of the compound within seventy-two hours after its administration so that, as previously stated, we have estimated the maximal single tolerated dose by this route of administration to be about 0.9 Gm. per kilogram.

TABLE 2.—*Single Intravenous Injection of Tryparsamide in the Treatment of Acute Syphilitic Orchitis of Rabbits*

No.	Dose, Gm. per Kg.	Results of Dark Field Examinations for T. Pallidum, Days *													Results of Transfer of Lymph Nodes
		1	2	3	7	14	21	28	35	42	49	56	63	70	
1	0.1	4	4	4	4	4	4	3	3	4	4	3	4	4	Positive
2	0.1	4	4	4	4	4	4	4	3	3	3	4	4	4	Positive
3	0.2	4	1	—	4	4	3	3	4	4	4	3	4	4	Positive
4	0.2	4	2	—	3	4	4	4	3	3	4	4	4	4	Positive
5	0.3	4	—	—	—	3	4	4	4	3	3	3	4	4	Positive
6	0.3	4	—	—	1	3	3	4	4	4	3	3	4	4	Positive
7	0.4	2	—	—	—	—	—	—	—	—	—	4	4	4	Positive
8	0.4	1	—	—	—	—	—	—	—	—	—	2	4	4	Positive
9	0.5	—	—	—	—	—	—	—	—	—	—	—	—	—	Positive
10	0.5	—	—	—	—	—	—	—	—	—	—	—	—	—	Positive
11	0.6	—	—	—	—	—	—	—	—	—	—	—	—	—	Negative
12	0.6	—	—	—	—	—	—	—	—	—	—	—	—	—	Positive
13	0.8	—	—	—	—	—	—	—	—	—	—	—	—	—	Negative
14	0.8	—	—	—	—	—	—	—	—	—	—	—	—	—	Negative
15	1.0	—	—	D	..	..	..	..	..	..	..	..	..	..	.....
16	1.0	—	D	..	..	..	..	..	..	..	..	..	..	..	.....

* After institution of treatment: 4 indicates large number of actively motile spirochetes per dark field; 3, 2 and 1 indicate smaller numbers of spirochetes per dark field, respectively; — indicates negative results on dark field examinations; D indicates death of animal.

Single Intramuscular Injections of Penicillin and Intravenous Injections of Tryparsamide.—As shown in table 3, rabbits were given single doses of penicillin by intramuscular injection in amounts varying from 1,000 to 300,000 units per kilogram of body weight. At the same time all animals were given 0.05 Gm. of tryparsamide by intravenous injection, which dose was about one-twelfth the single minimal curative dose by this route of administration. The single minimal curative dose of penicillin, however, was about 200,000 units per kilogram, so that the simultaneous administration of tryparsamide in a dose of 0.05 Gm. per kilogram was without demonstrable synergistic or additive spirocheticidal activity.

Multiple Intramuscular Injections of Penicillin.—We have previously reported [3] that the minimal curative dose of penicillin by intra-

muscular injection once daily for eight days in succession was approximately 5,000 units per kilogram, for a total of 40,000 units. In this investigation 1 of 2 rabbits given 2,000 units per kilogram once

TABLE 3.—*Single Intramuscular Injections of Penicillin in Isotonic Solution of Sodium Chloride with Single Intravenous Injections of Tryparsamide in the Treatment of Acute Syphilitic Orchitis of Rabbits*

No.	Penicillin, Units per Kg.	Tryparsamide Gm. per Kg.	Results of Dark Field Examinations for T. Pallidum, Days *													Results of Transfer of Lymph Nodes
			1	2	3	7	14	21	28	35	42	49	56	63	70	
1	1,000	0.05	4	4	4	4	4	4	4	4	3	3	4	4	4	Positive
2	1,000	0.05	4	4	4	4	4	4	3	4	3	4	4	4	4	Positive
3	5,000	0.05	4	4	4	4	4	4	4	3	3	3	4	4	4	Positive
4	5,000	0.05	4	4	4	4	4	4	4	4	3	3	4	4	4	Positive
5	10,000	0.05	2	—	—	—	4	4	4	3	4	3	3	4	4	Positive
6	10,000	0.05	2	—	—	—	3	4	4	3	3	3	3	4	4	Positive
7	25,000	0.05	1	—	—	—	—	—	4	4	3	3	4	4	4	Positive
8	25,000	0.05	1	—	—	—	—	—	3	4	4	3	3	4	4	Positive
9	50,000	0.05	1	—	—	—	—	—	—	—	4	4	3	3	4	Positive
10	50,000	0.05	1	—	—	—	—	—	—	—	4	3	3	3	4	Positive
11	100,000	0.05	1	—	—	—	—	—	—	—	—	—	3	4	4	Positive
12	100,000	0.05	1	—	—	—	—	—	—	—	—	—	4	4	4	Positive
13	200,000	0.05	—	—	—	—	—	—	—	—	—	—	—	—	—	Negative
14	200,000	0.05	—	—	—	—	—	—	—	—	—	—	—	—	—	Positive
15	300,000	0.05	—	—	—	—	—	—	—	—	—	—	—	—	—	Negative
16	300,000	0.05	—	—	—	—	—	—	—	—	—	—	—	—	—	Negative

* After institution of treatment: 4 indicates large numbers of actively motile spirochetes per dark field examination; 3, 2 and 1 indicate smaller numbers of spirochetes per dark field respectively; — indicates negative results in dark field examinations.

TABLE 4.—*Multiple Intramuscular Injections of Penicillin in Isotonic Solution of Sodium Chloride in the Treatment of Acute Syphilitic Orchitis of Rabbits*

No.	Dose *		Dose †		Results of Dark Field Examinations for T. Pallidum, Days ‡													Results of Transfer of Lymph Nodes
	Units per Kg.	Total	Units per Kg.	Total	1	2	3	7	14	21	28	35	42	49	56	63	70	
1	500	4,000	...	.....	4	2	1	—	—	—	—	2	4	4	4	4	4	Positive
2	500	4,000	...	.....	4	2	—	—	—	—	—	2	4	4	4	4	4	Positive
3	1,000	8,000	...	.....	4	2	—	—	—	—	—	—	2	4	4	4	4	Positive
4	1,000	8,000	...	.....	4	1	—	—	—	—	—	—	—	4	4	4	4	Positive
5	2,000	16,000	...	.....	4	1	—	—	—	—	—	—	—	—	—	—	—	Negative
6	2,000	16,000	...	.....	4	1	—	—	—	—	—	—	—	—	—	2	2	Positive
7	5,000	40,000	...	.....	4	1	—	—	—	—	—	—	—	—	—	—	—	Negative
8	5,000	40,000	...	.....	4	1	—	—	—	—	—	—	—	—	—	—	—	Negative
9	.....	.....	250	4,000	4	4	4	1	—	—	—	—	—	—	4	4	4	Positive
10	.....	.....	250	4,000	4	4	4	2	—	—	—	—	—	3	4	4	4	Positive
11	.....	.....	500	8,000	4	3	1	—	—	—	—	—	—	—	—	—	—	Negative
12	.....	.....	500	8,000	4	4	1	—	—	—	—	—	—	—	—	—	—	Negative
13	.....	.....	1,000	16,000	4	1	—	—	—	—	—	—	—	—	—	—	—	Negative
14	.....	.....	1,000	16,000	4	1	—	—	—	—	—	—	—	—	—	—	—	Negative

* Given once daily for eight days in succession.
† Given twice daily for eight days in succession.
‡ After institution of treatment: 4 indicates large numbers of actively motile spirochetes per dark field; 3, 2 and 1 indicate smaller number of spirochetes per dark field, respectively; — indicates negative results on dark field examinations.

a day for eight days in succession, a total of 16,000 units, showed complete or biologic cure, while both of 2 rabbits given 5,000 units per kilogram once a day for eight days in succession, for a total of 40,000 units, showed complete or biologic cure (table 4). When given twice

daily (8 a. m. and 3 p. m.) for eight days in succession the minimal curative dose was found to be approximately 500 units per kilogram, for a total of 8,000 units (table 4), which was likewise the minimal curative dose previously reported for this method of administration.[4]

Multiple Intravenous Injections of Tryparsamide.—As shown in table 5, however, the intravenous injection of tryparsamide in amounts

TABLE 5.—*Multiple Intravenous Injections of Tryparsamide in the Treatment of Acute Syphilitic Orchitis of Rabbits*

No.	Dose, Gm. per Kg.*	Total Dose, Gm. per Kg.	Results of Dark Field Examinations for T. Pallidum, Days †													Results of Transfer of Lymph Nodes
			1	2	3	7	14	21	28	35	42	49	56	63	70	
1	0.02	0.16	4	4	4	4	4	4	4	4	4	3	3	4	4	Positive
4	0.05	0.4	4	4	4	4	4	4	4	4	3	3	4	4	4	Positive
2	0.02	0.16	4	4	4	4	4	4	4	4	3	3	3	4	4	Positive
3	0.05	0.4	4	4	4	4	4	4	4	3	3	3	4	4	4	Positive
5	0.1	0.8	4	4	4	1	—	—	3	4	4	4	3	3	4	Positive
6	0.1	0.8	4	4	4	1	—	—	4	4	4	3	3	4	4	Positive
7	0.2	1.6	4	—	—	—	—	—	—	—	—	—	—	—	—	Positive
8	0.2	1.6	4	1	—	—	—	—	—	—	—	—	—	—	—	Positive

* Administered once a day for eight days in succession.
† After institution of treatment: 4 indicates large numbers of actively motile spirochetes per dark field; 3, 2 and 1 indicate smaller numbers of spirochetes per dark field, respectively; — indicates negative results on dark field examinations.

TABLE 6.—*Multiple Intramuscular Injections of Penicillin in Isotonic Solution of Sodium Chloride and Intravenous Injections of Tryparsamide in the Treatment of Acute Syphilitic Orchitis of Rabbits*

No.	Tryparsamide *		Penicillin *		Results of Dark Field Examinations for T. Pallidum, Days †													Results of Transfer of Lymph Nodes
	Gm. per Kg.	Total	Units per Kg.	Total	1	2	3	7	14	21	28	35	42	49	56	63	70	
1	0.05	0.4	100	800	4	4	4	2	2	—	—	—	—	—	—	—	—	Positive
2	0.05	0.4	100	800	4	4	3	3	—	—	—	—	—	—	—	—	—	Positive
3	0.05	0.4	250	2,000	4	2	—	—	—	—	—	—	—	—	—	—	—	Positive
4	0.05	0.4	250	2,000	4	2	—	—	—	—	—	—	—	—	—	—	—	Positive
5	0.05	0.4	500	4,000	4	4	1	—	—	—	—	—	—	—	—	—	—	Negative
6	0.05	0.4	500	4,000	4	4	2	—	—	—	—	—	—	—	—	—	—	Negative
7	0.05	0.4	1,000	8,000	4	2	—	—	—	—	—	—	—	—	—	—	—	Negative
8	0.05	0.4	1,000	8,000	4	1	—	—	—	—	—	—	—	—	—	—	—	Negative

* Administered once daily for eight days in succession.
† After institution of treatment: 4 indicates large numbers of actively motile spirochetes per dark field; 3, 2 and 1 indicate smaller numbers of spirochetes per dark field, respectively; — indicates negative results on dark field examinations.

varying from 0.02 to 0.2 Gm. per kilogram of body weight once a day for eight days in succession, totaling from 0.16 to 1.6 Gm. per kilogram, did not result in complete or biologic cures although evidences of spirocheticidal activity were apparent on the basis of the results of dark field examinations for T. pallidum.

4. Kolmer, J. A., and Rule, A. M.: Penicillin in the Treatment of Experimental Syphilis of Rabbits: V. The Synergistic or Additive Activity of Penicillin Injected Intramuscularly with Sodium Iodide Administered Orally and Intravenously, Arch. Dermat. & Syph., this issue, p. 49.

Multiple Intramuscular Injections of Penicillin and Intravenous Injections of Tryparsamide.—But while single doses of penicillin and tryparsamide administered at the same time were without synergistic or additive spirocheticidal activity, multiple doses of both compounds have shown these effects. Thus, as shown in table 6, the curative dose of penicillin once a day for eight days in succession was reduced from approximately 2,000 units per kilogram, with a total of 16,000 units (table 4), to approximately 500 units per kilogram, with a total of 4,000 units, when administered at the same time with intravenous injections of tryparsamide in a dose of 0.05 Gm. per kilogram, once a day for eight days in succession, for a total of 0.4 Gm.

Curiously enough, however, when penicillin was given twice daily (10 a. m. and 3 p. m.) by intramuscular injection for eight days in

TABLE 7.—*Multiple Intramuscular Injections of Penicillin in Isotonic Solution of Sodium Chloride and Intravenous Injections of Tryparsamide in the Treatment of Acute Syphilitic Orchitis of Rabbits*

	Tryparsamide *		Penicillin †		Results of Dark Field Examinations for T. Pallidum, Days ‡												Results of Transfer of Lymph Nodes
No.	Gm. per Kg.	Total	Units per Kg.	Total	1	2	3	7	14	21	28	35	42	49	56	63	70	
1	0.05	0.4	100	1,600	4	4	4	—	—	—	—	—	—	—	4	4	4	Positive
2	0.05	0.4	100	1,600	4	4	4	—	—	—	—	—	—	1	4	4	4	Positive
3	0.05	0.4	250	4,000	4	4	4	—	—	—	—	—	—	—	—	—	4	Positive
4	0.05	0.4	250	4,000	4	4	4	—	—	—	—	—	—	—	—	2	4	Positive
5	0.05	0.4	500	8,000	4	2	—	—	—	—	—	—	—	—	—	—	—	Negative
6	0.05	0.4	500	8,000	4	1	—	—	—	—	—	—	—	—	—	—	—	Negative
7	0.05	0.4	1,000	16,000	4	—	—	—	—	—	—	—	—	—	—	—	—	Negative
8	0.05	0.4	1,000	16,000	3	—	—	—	—	—	—	—	—	—	—	—	—	Negative

* Administered once daily for eight days in succession.
† Administered twice daily for eight days in succession.
‡ After institution of treatment: 4 indicates large numbers of actively motile spirochetes per dark field; 3, 2 and 1 indicate smaller numbers of spirochetes per dark field, respectively; — indicates negative results on dark field examinations.

succession, along with tryparsamide once a day by intravenous injection, there were no appreciable synergistic or additive spirocheticidal effects. Thus, as was previously stated, the minimal curative dose of penicillin by this method of treatment was approximately 500 units per kilogram (a total of 8,000 units). This dose, however, was not reduced by the administration of 0.05 Gm. of tryparsamide per kilogram once a day during the period of treatment (table 7).

SUMMARY

The single minimal curative dose of commercial penicillin injected intramuscularly in isotonic solution of sodium chloride in the treatment of acute syphilitic orchitis of rabbits was approximately 200,000 units per kilogram of body weight.

The single minimal curative dose of tryparsamide injected intravenously was about 0.6 Gm. per kilogram of body weight. The single

maximal tolerated dose by this route of administration was about 0.9 Gm. per kilogram, the chemotherapeutic index thus being 1.5.

The intravenous injection of 0.05 Gm. of tryparsamide per kilogram had no appreciable synergistic or additive spirocheticidal effects on the single minimal curative dose of penicillin injected intramuscularly.

The minimal curative dose of penicillin administered once daily for eight days in succession was about 2,000 units per kilogram, for a total of 16,000 units.

The intravenous administration of tryparsamide once a day for eight days in succession in doses varying from 0.02 to 0.2 Gm. per kilogram, for a total of 0.16 to 1.6 Gm., was not completely curative.

The intravenous administration of tryparsamide, however, once a day for eight days in succession in a dose of 0.05 Gm. per kilogram (a total of 0.4 Gm.), reduced the minimal curative dose of penicillin injected intramuscularly once a day for eight days in succession from approximately 2,000 units per kilogram (a total of 16,000 units) to approximately 500 units per kilogram (a total of 4,000 units).

The minimal curative dose of penicillin given by intramuscular injection twice daily for eight days in succession was approximately 500 units per kilogram (a total of 8,000 units). When the penicillin was administered along with tryparsamide given by intravenous injection in a dose of 0.05 Gm. per kilogram once daily for eight days in succession, the minimal curative dose of penicillin, however, was approximately the same.

Under the circumstances it appears that combined treatment of acute syphilitic orchitis of rabbits with penicillin and tryparsamide may show some degree of synergistic or additive spirocheticidal activity but that these effects are not nearly as pronounced as those in combined treatment with penicillin and oxophenarsine hydrochloride (mapharsen®) or in combined treatment with penicillin and bismuth.

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SJÖGREN'S SYNDROME

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AND
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THIS REPORT is the first one in the American dermatologic literature of a case of Sjögren's syndrome. This rare systemic disorder combines a group of functional disturbances affecting embryologic derivants of ectodermal and entodermal tissue. The cause is as yet unknown, but has been believed to be related to vitamin A and B deficiency as well as to disturbances in mineral metabolism and endocrine function. In view of these theoretic possibilities, the patient described in this report was admitted to the Mount Sinai Hospital, where extensive studies were performed in an attempt to elucidate fundamental causative factors.

REPORT OF A CASE

History.—B. R., a 43 year old white woman, was first seen in the Mount Sinai Hospital in 1929 owing to profuse, irregular vaginal bleeding for one year. A large submucous fibroma was found projecting through the cervix. An avulsion of the submucous, pedunculated fibroma was done. The patient recovered from the operation uneventfully and was discharged.

In December 1947, when she was aged 61, she was admitted to the hospital for the second time, with the chief complaints of dryness of the mouth, nose, ears and eyes of five years' duration. She also gave a history of arthritis involving the hands, wrists, elbows, knees and ankles, with recurrent exacerbations during the past forty years. She gave a history of Raynaud's phenomenon (numbness, pain and whiteness of all extremities when exposed to cold, and paresthesia of the hands and feet) for the past eighteen years. About five years before, the patient had noted an extreme dryness of the mouth, tongue, nose and throat, with severe burning of the tongue and angles of the mouth. For the past two to three years, she had had severe dryness and burning of the eyes as well and had noted progressive dryness of the skin over the entire body. Her menopause had occurred in 1939. For all these complaints, she had been treated by a private physician for years with very large doses of multiple vitamins and dilute hydrochloric acid given by mouth, without result. She also gave a history of having had an episode, twelve years before, of enlargement of the right side of the face (parotid gland), with splitting of the skin at the corner of the mouth.

From the Department of Dermatology, service of Dr. Samuel Peck, Mount Sinai Hospital, New York.

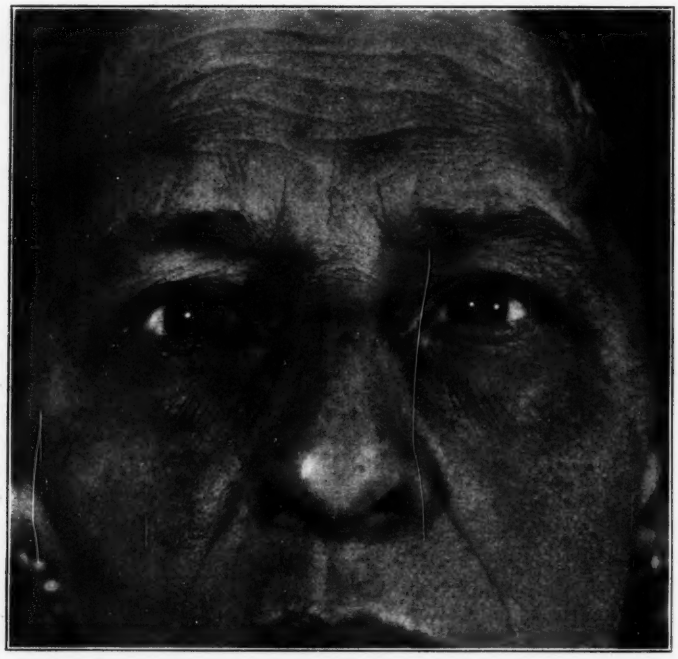

Fig. 1.—The conjunctival and lid margins appear extremely dry. It was not possible to demonstrate photographically the advanced dryness of the conjunctivas, which could actually be made to wrinkle under pressure.

Fig. 2.—Scrotal tongue. The lips show excessive dryness and wrinkling, with slight fissures at the angles of the mouth.

Examination of the patient showed a moderately developed and nourished, elderly white woman in no acute distress. Ophthalmologic examination revealed an injected, thickened conjunctiva with some papillary hypertrophy; some mucoidal secretion was present, and a slight amount of injection was seen perilimbally. The conjunctiva was so dry (fig. 1) that it could be wrinkled into folds with the slightest pressure. Gross examination of the cornea revealed some epithelial spots with attached filaments. The entire right cornea showed punctate epithelial erosion on staining with fluorescein; the left cornea showed less staining but more

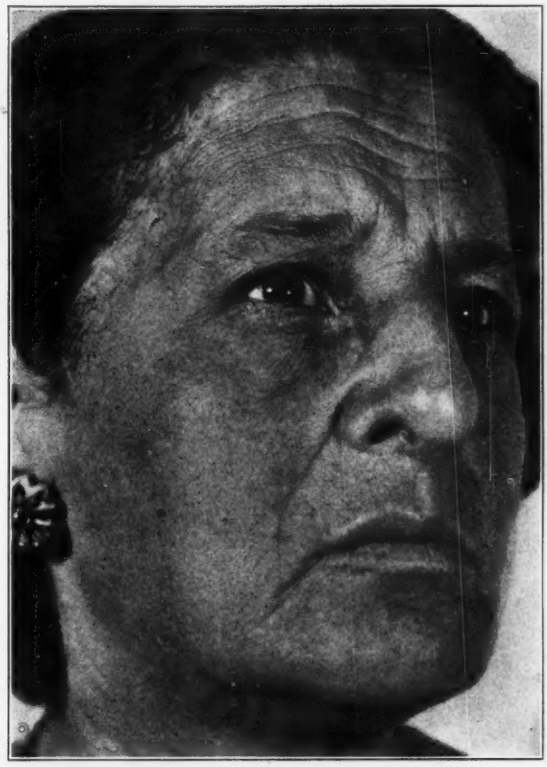

Fig. 3.—Fissuring of the angles of the mouth. The skin of the entire face is erythematous and asteatotic.

filaments. The test for tearing showed almost complete absence of secretion. The otolarynogologic examination revealed that the nasal mucosa was pale, with moderate polypoid changes of the mucosa of the middle turbinate body and moderate crusting of the septum. The nasopharyngeal mucosa was extremely pale. A similar pallor and extreme xerostomia was noted on the buccal mucosa and uvula. The tongue was very dry and of a scrotal type (fig. 2). The skin was erythematous and fissured (perlèche) at both angles of the mouth (fig. 3). Small,

pea-sized nodes were felt at the posterior cervical and left axillary regions. The skin of the entire body was dry, with some excoriations on the chest and neck. A few erythematous papules varying from 0.5 to 1 cm. in size were noted on the right side of the neck (fig. 4), where the patient claimed that she had been bitten by a caterpillar years ago. The heart was not enlarged; a harsh, blowing systolic

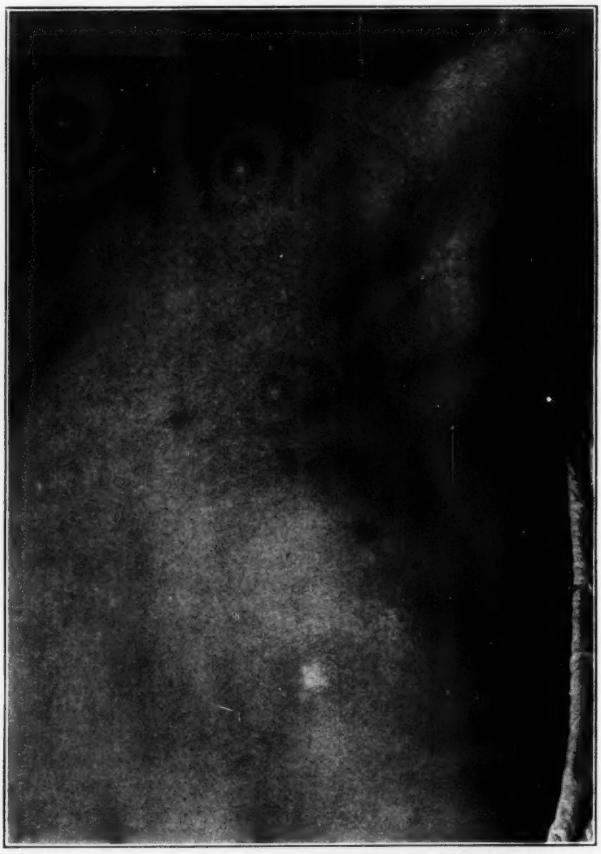

Fig. 4.—Right side of the neck and shoulder, showing dryness of skin, few excoriations and several shiny papules (histologic aspect that of granuloma annulare).

murmur was heard over the aortic area. A moderate degree of sclerosis was noticed over the palpable arteries. The abdomen was essentially normal.

Laboratory Observations.—The blood count revealed 14.5 Gm. of hemoglobin. The red blood cell count was 4,900,000. The platelet count was 160,000. The white blood cell count was 7,300, with 61 per cent segmented neutrophils, 8 per

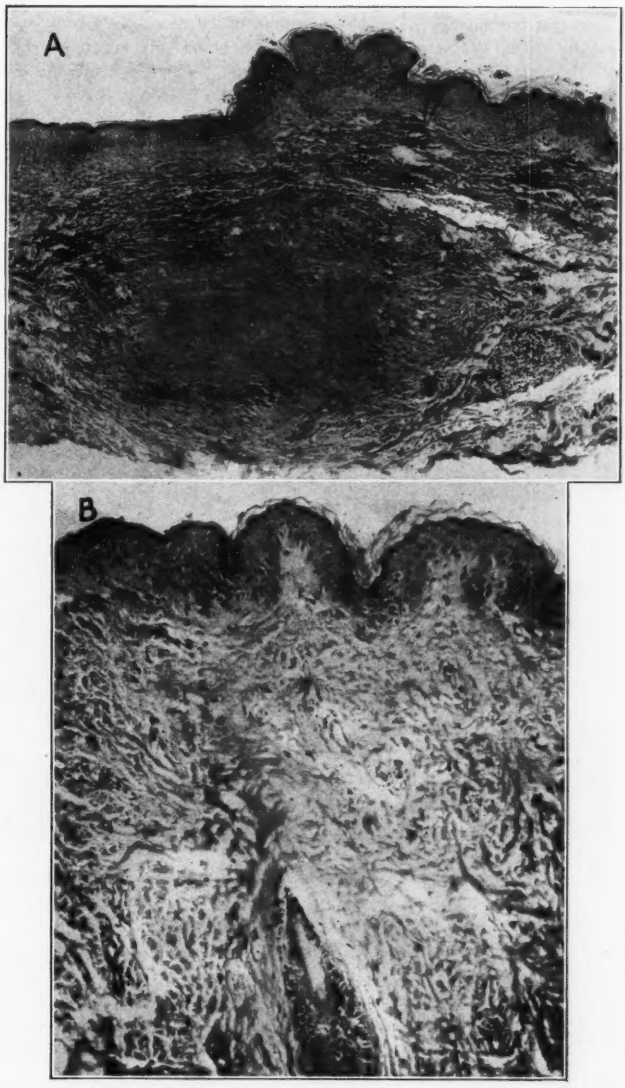

Fig. 5.—Magnifications of skin from a papule in the neck. The skin shows a circinate infiltration of histiocytes in the upper portion of the corium, with a clear, more or less homogeneous central degeneration of collagen. *A* is a low power view (× 30), and *B*, a medium power one (× 222).

cent nonsegmented neutrophils, 22 per cent lymphocytes, 5 per cent monocytes and 4 per cent eosinophils. The blood sedimentation rate was 8 mm. at the end of one hour. The Wassermann reaction of the blood was negative. The blood chemistry revealed 14 mg. of urea nitrogen, 2.8 mg. of uric acid, 75 mg. of sugar, 620 mg. of chlorides (as sodium chloride), 2.1 mg. of phosphorus, 11.2 mg. of calcium and 300 mg. of cholesterol per hundred cubic centimeters, with 4.6 Gm. of albumin and 2.6 Gm. of globulin, with a total amount of protein of 7.3 Gm. Reactions to the formol gel test were negative. The coagulation time was eight minutes. The bleeding time was two minutes. The gastric analysis revealed no free acid and a very low total acidity (16 millimole concentration being the highest). There was no response to the injection of histamine. An electrocardiogram revealed no abnormal tracings. The pancreatic and gallbladder functions were normal. A vitamin A tolerance test revealed a normal vitamin level and a normal absorption

Fig. 6.—A high power (× 500) view of the specimen seen in figure 5.

curve. The basal metabolic rate was determined to be + 25 per cent. Roentgenologic examination of the skull and bones revealed normal conditions. Physiologic sweating tests revealed no abnormality of sweat secretion. Pilocarpine (15 mg.) was given orally and produced some sweating on the face and hands but no salivation. The left parotid duct was canalized with a no. 19 blunt needle, and 8 mg. of pilocarpine injected hypodermically produced no salivation from either parotid gland and no perspiration of the facial skin. Two biopsies (by Dr. C. F. Sims) of the cutaneous lesion on the right side of the neck (figs. 5 and 6) revealed circinate infiltration in the upper portion of the corium, with a clear, more or less homogeneous center. The diagnosis of granuloma annulare was made on two occasions. Histologic examination of the buccal mucosa (figs. 7 and 8) showed slight superficial inflammation. Histologic examination of tissue from the

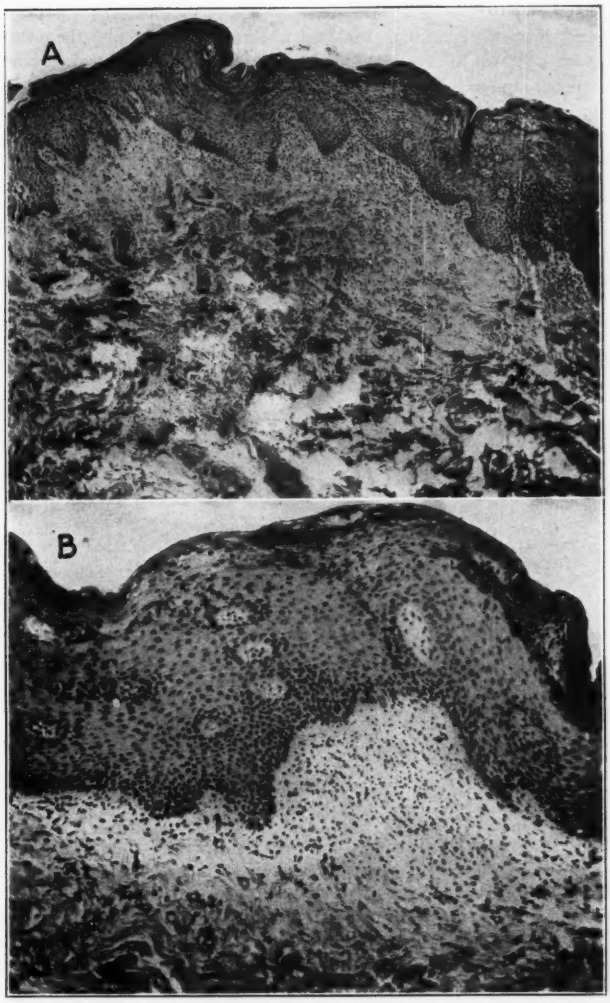

Fig. 7.—Magnifications of tissue from the buccal mucosa, showing mild acanthosis, dilatation of superficial blood vessels and mild cellular infiltration. *A* is a low power view (× 30), and *B*, a medium power one (× 222).

vaginal mucosa showed slight irregular acanthosis, intercellular edema and dilated vessels, and the condition was reported as superficial vaginitis. A vaginal smear was reported as showing normal menopausal changes and shrinkage of the cells (figs. 9 and 10).

Course.—For the immediate relief of the ocular symptoms, the patient was treated with a heated pin, with the use of procaine under (novocain®) anesthesia, and the upper and lower puncta and canaliculi were closed. There was some improvement in the symptoms of dryness of the eyes, but it was temporary. The patient was then given 100,000 units of a preparation containing vitamin A intra-

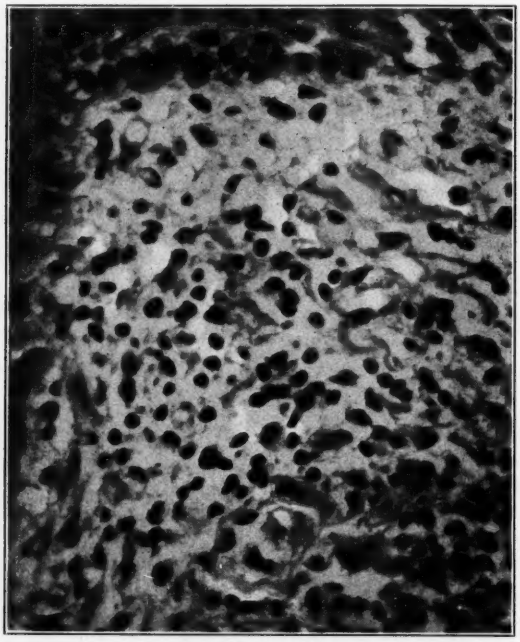

Fig. 8.—A high power (× 500) view of the specimen shown in figure 7.

muscularly every day, with large amounts of all vitamins orally four times a day. In addition she received 100 mg. of nicotinic acid and 100 mg. of thiamine hydrochloride intravenously twice weekly for a period of thirty-five days, with no apparent improvement either subjectively or objectively. She was then given 10,000 rat units of estrogen three times a week for two weeks, followed by 50,000 units intramuscularly every day for fourteen days, with no apparent results, although the vaginal smear revealed a very good vaginal response The administration of estrogen was discontinued because of the development of anxiety and a sense of restlessness on the part of the patient. She was again given four multivitamin tablets three times a day plus dilute hydrochloric acid, 10 drops three times a day before meals, and crude liver extract, 2 cc. intramuscularly three times a week.

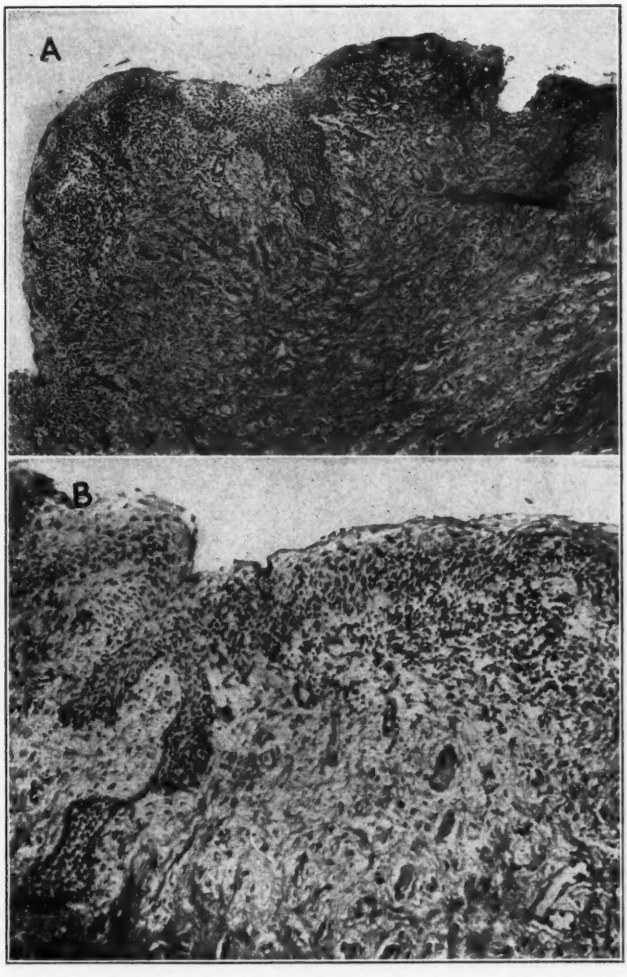

Fig. 9.—Magnifications of vaginal tissue, showing mild, irregular acanthosis, intercellular edema and dilated vessels.

The patient was discharged from the hospital, with instructions to continue the same treatment as an ambulatory patient. She has been followed in the clinic for four months, and there has been practically no change in her condition.

HISTORICAL ACCOUNT OF THE SYNDROME

In 1933, Sjögrèn [1] described a chronic disorder characterized by lessened or absent secretions of the salivary and lacrimal glands, with accompanying dryness of the eyes, mucous membranes of the mouth and the upper respiratory tract. The dryness of the eyes had just been recognized as a cause of certain cases of keratitis by Stock [2] in 1924.

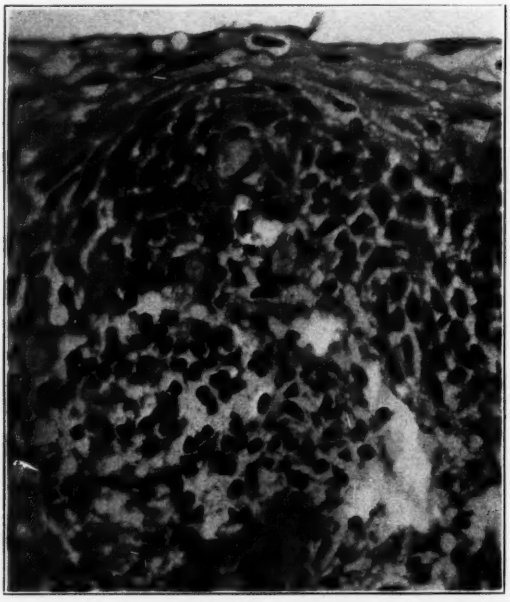

Fig. 10.—A high power (× 500) view of the tissue seen in figure 9.

This type of dryness was termed "keratoconjunctivitis sicca" by Duke-Elder [3] in 1930 and was suspected by several investigators of being a manifestation of an underlying systemic disturbance. The several publications of Sjögren [4] established the condition as a syndrome

1. Sjögren, H.: Acta ophth., 1933, supp. 2, p. 1.

2. Stock, in von Graefe, A., and Saemisch, E. T.: Handbuch der gesamten Augenheilkunde, Leipzig, Wilhelm Engelmann, 1924.

3. Duke-Elder, W. S.: Brit. J. Ophth. **14**:61, 1930.

4. Sjögren, E.: (*a*) Footnote 1; (*b*) Acta ophth. **16**:70, 1938; (*c*) A New Conception of Keratoconjunctivitis Sicca (Keratitis Filiformis in Hypofunction of the Lachrymal Glands), Sydney, Australasian Med. Pub. Co., Ltd., 1943.

incorporating the manifestations of keratoconjunctivitis sicca, laryngopharyngitis sicca and enlargement of the parotid glands.

ETIOLOGY

MacLean [5] stated in his excellent article on this disease, as first observed by Albrich,[6] that there is no satisfactory explanation of this syndrome. It is apparently a general systemic disturbance involving the lacrimal and salivary glands and frequently associated with other evidences of a chronic systemic infection, such as arthritis, anemia, lymphocytosis and increased sedimentation rate. In addition to these manifestations, some patients have shown a diminished naso-ocular reflex, a peculiar xerosis of the upper respiratory tract, achylia and suppression of excretion of sweat. These symptoms led the Dalsgaard-Nielsens [7] and Bruce [8] to ascribe the condition to a disturbance of the sympathetic nervous system. Because of the similarity of the ocular lesions to those of xerophthalmia, the condition has been thought by some to be due to an avitaminosis. In 1 of the cases described by MacLean [5] an earlier medical diagnosis of avitaminosis had been made, but liberal amounts of vitamins failed to prevent development of the classic clinical picture of Sjögren's syndrome. Of course, the occurrrence of dryness of mucous membranes and cutaneous surfaces invariably raises the hue and cry of avitaminosis at the present time. When some of these so-called avitaminoses are well studied, the omnipresent diagnosis of vitamin deficiency vanishes into thin air. Our patient showed no signs of avitaminosis either from a standpoint of laboratory or of clinical investigation or from that of a response to adequate therapeutic intake. With extreme dryness of the salivary secretion as well as gastric achylia, a diminished absorption of vitamins and all foods would certainly be expected, but this could not be established.

Of interest relevant to this question are the cases observed by Lutman and Favata.[9] In their first case the vitamin A level of the blood and the vitamin A absorption curve were normal. In their second case both the vitamin A level of the blood and the absorption curve were low; the biophotometric measurements were within normal

5. MacLean, A. L.: Bull. Johns Hopkins Hosp. **74**:219, 1944.

6. Albrich, K.: Arch. Ophth. **121**:402, 1928.

7. Dalsgaard-Nielsen, E., and Dalsgaard-Nielsen, T.: Ugesk. f. læger **99**: 219, 1937.

8. Bruce, G. M.: Tr. Am. Ophth. Soc. **38**:149, 1940.

9. Lutman, F. C., and Favata, B. V.: Keratoconjunctivitis Sicca and Buccoglosso-Pharyngitis Sicca with Enlargement of Parotid Glands: Report of Two Cases of Sjögren's Syndrome, with Pathologic Study of Lacrimal Gland and Parotid Glands in One Case, Arch. Ophth. **35**:227 (March) 1946.

limits. Other evidences of vitamin A deficiency were not clinically outstanding. The presence of avitaminosis A was suspected and carefully investigated by them because of previous reports of vitamin A deficiency in the literature. Acknowledging this controversy concerning the etiologic factors, Jeghers [10] included Sjögren's syndrome with disorders due to vitamin A deficiency, largely on the strength of Stahel's [11] case, in which improvement followed vitamin A therapy. This case was complicated by advanced polyarthritis deformans. Bruce [8] also failed to find biophotometric evidence of vitamin A deficiency in his most typical case; Gifford, Puntenney and Bellows,[12] finding no deficiency of vitamin A in the blood in some of their cases, expressed the belief that vitamin A was rarely, if ever, a factor in the condition. As Marrack [13] observed, one of the cardinal changes that are seen in animals deprived of vitamin A is keratinizing metaplasia of epitheliums. The epithelium in, for example, the cornea is replaced by a stratified, keratinized epithelium. The change is reversible; when the animals are treated with vitamin A, fresh epithelial cells are formed that have the structure and functions of the original epithelial cells. One may suppose that vitamin A is one of the balancing factors that control the development of epithelium and that a change toward the formation of keratinized epithelium may result from deficiency of vitamin A or from excessive action of other factors. Marrack further stated that keratinizing metaplasia in human beings has been attributed primarily to deficiency of vitamin A; in some instances the evidence of the deficiency has not been convincing. On the other hand, investigators dealing with morbid anatomy commonly hold that this metaplasia is produced by irritation or inflammation. It seems that there have been no adequate investigations concerning the evidence of this type of metaplasia in subjects not suspected of deficiency. Much remains to be learned about the metabolism of vitamin A—its absorption, its storage and mobilization, its transfer from plasma to tissues and its utilization or mode of action in cells. Many are too likely to incriminate all diseases of the skin characterized by dryness of the skin and keratosis of the hair follicle as related to a deficiency of vitamin A. From the present evidence, it must be concluded that avitaminosis A is an inconstant finding in cases of Sjögren's syndrome.

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10. Jeghers, H.: New England J. Med. **228**:715, 1943.

11. Stahel, W.: Klin. Wchnschr. **17**:1692, 1938.

12. Gifford, S. R.; Puntenney, T., and Bellows, T. G.: Tr. Am. Ophth. Soc. **41**:80, 1942.

13. Marrack, J. R., in MacKenna, R. M. B.: Modern Trends in Dermatology, New York, Paul B. Hoeber, Inc., 1948.

Lutman and Favata [9] also observed that in 2 of their cases there was an implication of a deficiency of members of the vitamin B complex, with many of the signs and symptoms attributed to an extreme degree of ariboflavinosis. Because of the presence of these signs, their 2 patients received treatment repeatedly, although unsuccessfully, with yeast, concentrates of the vitamin B complex and riboflavin. Our patient was similarly and unsuccessfully treated. The assumption being that the signs were caused by a lack of riboflavin, there might exist, however, a faulty absorption of this vitamin in the intestinal tract or an inability to utilize it. An inadequate diet alone could modify or contribute to such a deficiency but would not satisfactorily explain the predominance of the reported cases of this disease in women unless some further factor of sex is responsible. No studies of the incidence of ariboflavinosis relative to sex are available. Twenty-one of the group of 29 hospitalized patients and outpatients presented by Sydenstricker and associates [14] as manifesting riboflavin deficiency were women. This series, admittedly, is too small to permit more than suggestive conclusions.

That the endocrine system may also play a part in the production of the symptoms has long been suspected. As most cases occur in women usually at or near the menopause, a deficiency of estrogenic hormones has been considered by many authors as a possible etiologic factor. The condition does occur, however, before the climacteric. MacLean [5] reported a case in which the symptoms developed long before this period and in which the menstrual flow was normal. In his first case, however, the symptoms commenced when the patient was 25, five years after panhysterectomy with artificial menopause. Hossos (cited by von Grósz [15] and Bruce [8]) removed the lacrimal glands from a rabbit, but no keratitis appeared until the ovaries also were removed. Krasso [16] reported the onset of keratoconjunctivitis sicca following oophorectomy. Lisch,[17] on the other hand, pointed out that the signs of glandular involvement sometimes antedate the appearance of the ocular symptoms by several years and that the association of the menopause with the appearance of the symptoms in the eyes may be entirely coincidental.

In the patient described in this report, the majority of the signs and symptoms appeared around the time of menopause. Vaginal smears performed during her hospital stay showed the usual menopausal changes. She was treated with large doses of estrogen, with reversion of the vaginal smears to the normal premenopausal status. Outside of this

14. Sydenstricker, V. P.; Sebrell, W. H.; Cleckley, H. M., and Kruse, H. D.: The Ocular Manifestations of Ariboflavinosis, J. A. M. A. **114**:2437 (June 22) 1940.

15. von Grósz, S.: Klin. Monatsbl. f. Augenh. **97**:472, 1936.

16. Krasso, I.: Ztschr. f. Augenh. **61**:1, 1930.

17. Lisch, K.: Arch. f. Augenh. **110**:357, 1937.

laboratory finding, there was no apparent subjective or objective improvement in the condition of the patient. In fact, she became considerably agitated, and the medication had to be discontinued. If the estrogen deficiency were of a basic nature in this disease, the patient should have experienced some improvement in her condition after the large doses administered. This theory holds true especially in view of the development of a normal vaginal smear, which indicated that an adequate therapeutic level had been obtained. Nevertheless, the menopause has been assumed to play some role, inasmuch as the majority of patients have been women in that age group and estrogen deficiency is a not uncommon accompaniment of xerosis of the skin and mucous membranes. There is a small fly in this potpourri of accepted thought. Current research has shown that estrogens diminish keratinization and the activity of the sebaceous glands. If such is the case, why should estrogens be of value in treatment of this disease or keratoderma climacterium, pruritus vulvae (menopausal type) and kraurosis vulvae? On the other hand, androgens stimulate the surface epithelium and the sebaceous glands, leading to hyperkeratosis and seborrhea. These facts appear to be confusing and contradictory. In all probability, it is the ratio between circulating androgen and estrogen which is responsible for the aforementioned cutaneous changes, and it is this ratio which is influnced by therapy. In addition, the degree of sensitivity to hormonal influence varies from tissue to tissue and is also responsible for unexplained reactions. As is well known, only a small percentage of women have keratoderma of the palms and soles at the time of menopause. This condition probably indicates hypersensitiveness of these areas to the increased amount of circulatory androgen or to the disturbed androgen-estrogen balance of the menopausal period. In view of these unanswered questions, the patient observed in this study will be treated with androgens at an appropriate time in the future.

Other theories of interest include those of Sjögren,[4] who expressed the belief that the condition is due to an infection carried by the blood stream. Knapp [18] stated the opinion that the condition is a result of acute rheumatic fever. All 3 of the patients in the series reported by MacLean [5] had chronic rheumatoid arthritis. Bassalino [19] expressed the opinion that the syndrome is due to adrenal insufficiency.

SYMPTOMATOLOGY

The usual complaints are those of burning, pricking and smarting of the eyes and sometimes of diminished visual acuity, according to MacLean.[5] Frequently, but by no means invariably, this condition is

18. Knapp, P.: Klin. Monatsbl. Augenh. **82**:241, 1929.

19. Bassalino, G.: Boll. d'ocul. **15**:1193, 1936.

accompanied with dryness of the eyes. Photophobia is often present. The patients sometimes complain of the characteristic stringy, mucoid discharge and the difficulty in washing it away. Where the mucous is adherent to the bulbar conjunctiva it stains with argyrol® (a combination of silver with a protein produced by the electrolysis of serum albumin) or rose bengal and can readily be seen.

In 1943 Gifford, Puntenney and Bellows [12] classified cases with evidence of deficient lacrimation into three groups. In group 1, there was lacrimal deficiency, with moistening of less than 15 mm. in the Schirmer filter paper test after five minutes, but with no corneal or associated changes. In group 2, there was fairly complete lacrimal deficiency, with corneal and conjunctival changes of such a degree as to be visible only with the slit lamp and, as a rule, with no associated signs. Group 3 included cases of the typical Sjögren syndrome, with almost no lacrimal secretion in Schirmer's test and with conspicuous corneal and conjunctival changes and one or more of the extraocular signs of that syndrome, usually a deficiency of salivary secretion. The ocular condition sometimes does not appear for several years after the onset of the other symptoms, or it may be the only sign of the disease; when present, however, it seems to cause the most distress. Dry, ropy secretion, with shreds adhering to the corneal epithelium, is a constant observation and is seen in practically no other condition. Fine epithelial filaments may be present. In most cases there is diffuse, irregular, superficial staining of the cornea when fluorescein or other stains are used. Often clear regions are seen between deeply stained areas. Sensitivity is usually diminished. The conjunctiva may appear almost normal but is usually congested, and a foamy secretion is often found at the canthi. The eyes sometimes look dry and may be flecked with meibomian secretion, but, more often, absence of moisture is not apparent on inspection. This absence can be determined by means of a special filter. Seldom is the bacterial flora found to be anything but normal. Complications are rare. Sjögren [4] noted an instance of pannus formation, and another of perforating ulcer. In 1 of Bruce's [8] patients a dense corneal opacity developed. In these patients, the various component parts of the upper respiratory tract are commonly involved. The lips and mouth are dry, with perlèche-like fissures at the angles, as in our patient.

The tongue in our patient was of a scrotal type and somewhat sensitive. One of the complications observed in other patients whose cases have been reported is advanced dental caries. Cheyne [20] showed that a disturbance of normal salivary flow in rats in which the salivary glands had been removed resulted in an increase of experimental caries directly

20. Cheyne, V. D.: Proc. Soc. Exper. Biol. & Med. **42**:587, 1939.

in proportion to the amount of serous saliva removed. Lutman and Favata [9] observed that the early age at which dental caries occurred, requiring total extraction of the teeth in their first case when the patient was 28 and in their second case when the patient was 35, suggests that there was decreased salivation of a degree sufficient to produce dental caries even before the symptoms of a dry mouth were manifest to the patient. Pathologic changes in the salivary glands of these 2 patients may therefore have long antedated their first symptoms.

The parotid glands undergo a gradual, firm and painless swelling. The swelling may be permanent. Since the parotid gland is the main source of serous saliva and since the parenchyma of these glands is destroyed, there is little wonder that one of the most annoying complaints is a dry mouth. The lacrimal gland can also be expected to function poorly because of chronic changes in glandular structure. The infiltration of lymphoid cells, with changes in the connective tissue and destruction of the parenchyma of these glands, is the characteristic pathologic feature of this disease. If similar abnormalities exist in the epithelium and the glandular structures throughout the intestinal tract, interference with normal digestion and normal alimentary absorption is to be expected. This should cause a variety of superimposed chronic deficiences, contributing to the complex clinical and laboratory picture. The chronic inflammation of the mucosa of the upper respiratory system, which is covered with a sticky mucous section, is probably shared by the accessory air sinuses and their drainage channels. Pansinusitis, eustachitis and mastoiditis occurred in cases reported by Bruce.[21] Apparently the otolaryngologist is consulted as frequently by these patients as is the ophthalmologist.

Other associated features include rheumatoid arthritis, usually of the extremities. Acrocyanosis and Raynaud's phenomenon were present in our patient. Anemia, achylia and achlorhydria have been reported and were present in this case. Xeroderma due to anhidrosis and asteatosis is frequently observed and was also present in this case. The histologic diagnosis of granuloma annulare in this case cannot be adequately explained. The lesion removed for examination was one of a group of papules on the right side of the neck. These papules had been present for many years after a supposed bite from a caterpillar.

PATHOLOGY

The microscopic pathology of the disease was carefully studied by Sjögren.[4] There are no other pathologic reports on this condition in the literature.

21. Bruce, G. M.: Keratoconjunctivitis Sicca, Arch. Ophth. **26**:945 (Dec.) 1941.

According to Sjögren, the lacrimal and salivary (parotid, submaxillary and sublingual) glands, in all cases examined at autopsy or by biopsy, showed striking atrophy and some chronic inflammation, with eosinophils and scarring. In some cases there was cystic dilatation of the ducts. No giant cells were found.

Cornea.—The epithelium was normal in some areas, thinned or absent in others. Where filaments occurred, they were formed of the external portions of the epithelial layer or of whole, desquamated epithelium. Connective tissue in growths beneath the epithelium and degenerated foci in the parenchyma were occasionally found.

Conjunctiva.—There was early destruction of elastic tissue and edema of the epithelium. In all the cases there was infiltration with round cells and eosinophils and scarring. The mucous glands (goblet cells) were lacking generally but were present in large numbers in the lower fornix.

TREATMENT

Attempts have been made to increase glandular secretion by the use of parasympathomimetic agents. Pilocarpine, in doses of 1/7 to 1/5 grain (9 to 12 mg.), two or three times daily, caused some improvement of symptoms in 1 of Gifford's [12] patients. Neostigmine (prostigmine®) has been used recently. In some patients it caused disturbing general symptoms and no increase in lacrimal secretion. Bellows [12] compared the rate of tear flow, as shown by repeated Schirmer tests, before and after one subcutaneous injection of neostigmine bromide in 13 patients, and then after oral use of the drug for one week on 5 patients. The response varied after both types of administration but was quite definite in a number of cases. Other forms of systemic treatment believed to be of some value in isolated instances were the use of thyroid extract in treatment of patients with low metabolic rates, estrogenic extract for women who had reached the menopause, vitamins when there was a history of dietary deficiency and liver and iron for patients with anemia. In the patient described in this report, the therapeutic response was a questionable one.

SUMMARY

A case of Sjögren's syndrome (keratoconjunctivitis sicca and xerostomia) is reported. The discussion includes a review of pertinent facts relevant to etiology, symptomatology, pathology and therapy. The fundamental causative factors can only be surmised at the present state of knowledge.

2 East 69th Street.

ARTERIOSCLEROSIS OBLITERANS AS A CAUSE OF ULCERS OF THE LEG

SEYMOUR I. SHAPIRO, M.D.
AND
RUBEN NOMLAND, M.D.
IOWA CITY

CHRONIC ulcers of the leg are a perennial problem in charity institutions. As one reads the literature on ulcers one gets the impression that most of these lesions are caused by varicose veins, thrombophlebitis, lymphatic stasis and similar disturbances of the non-arterial circulation, producing chronic stasis and finally ulceration. In a continuing study of ulcers of the leg, particularly their treatment,[1] it seemed to us that a large percentage of these ulcers were not caused by stasis, and so, about three years ago, we decided to study the peripheral arterial circulation in all patients with ulcers of the leg. Of 52 cases studied since then we found 10, or about 20 per cent, in which the chief, if not the only, cause of the ulceration was diminished arterial circulation due to obliterating arteriosclerosis.

Many years ago, Eloesser [2] emphasized the multiplicity of factors causing ulcers of the leg, and his was the first report we could find in which arterial occlusion was assigned its important place in the etiology of ulcers of the leg. He stated that 25 of 76 ulcers in his series were of arterial origin. More recently, Hines and Farber [3] reported that arteriolar occlusion, as shown by biopsy, caused ulceration of the leg. Most of their patients had severe hypertension, and none of our 10 patients,

From the Department of Dermatology and Syphilology, University Hospitals, the State University of Iowa.

1. Ringrose, E. J.: The Treatment of Large Stasis Ulcers by Pinch Skin Grafts, J. Iowa M. Soc. **33**:175 (April) 1943. Nomland, R., and Wallace, E. G.: Penicillin for Ulcers of Leg Treated by Pinch Grafts, J. A. M. A. **130**:563 (March 2) 1946.

2. Eloesser, L.: Leg Ulcer, S. Clin. North America **2**:537 (April) 1922.

3. Hines, E. A., Jr., and Farber, E. M.: Ulcer of the Leg Due to Arteriolosclerosis and Ischemia, Occurring in the Presence of Hypertensive Disease (Hypertensive-Ischemic Ulcers): A Preliminary Report, Proc. Staff Meet., Mayo Clin. **21**:337 (Sept. 4) 1946.

apparently, had this type of ulcer. While several additional writers,[4] in evaluating newer diagnostic and treatment methods, have recognized the occurrence of ischemic ulcers, in some cases designating the associated arterial occlusive disease, we could find no reports in which attention had been directed to a study of the arterial supply as part of the routine in diagnosing the cause of ulcers of the leg.

The diagnosis of arteriosclerosis obliterans in this series is based on history and objective findings; the simplest and most reliable procedure is the palpation of the pulses. Repeated attempts to find all possible pulses in the lower extremity should be made, and inability to palpate the pulses by an experienced person is one of the best signs of partial or complete closure of the arteries.

Oscillometric readings, which are not difficult to do, are reliable indications of deficiency of the arterial circulation and were performed routinely on most of our patients with ulcers of the leg. Readings were taken on both thighs and both calves, and those of less than 2 were considered to be indicative of arterial occlusion of significant degree. The readings were usually about the same in the unaffected leg as in the one with the ulcer, but in some instances the reading in the ulcerated leg was much lower than that in the nonulcerated one. In all patients in whom arterial occlusion was diagnosed the oscillometric reading was much below normal.

The appearance of the skin and nails is often distinctive in arterial occlusion. The skin is usually thin, shiny and atrophic, and the nails are often thick and dystrophic. Color changes in the foot are usually evident, with mottled redness on dependency and pallor on elevation, with slow return of redness after the return to dependent position. Gross temperature changes are often present, but determination of the temperature of the skin by means of the thermocouple is subject to great error unless the environmental temperature is kept constant, and this procedure is, therefore, impracticable. Roentgenograms of a leg taken to show calcification of the arteries are equivocal, but osteoporosis is of considerable significance.

Subjective sensations of arterial insufficiency consist in pain on exercise, which is usually in the nature of intermittent claudication. Because of the relative inactivity of the age group subject to arteriosclerosis obliterans, this finding is not a constant one but does occur in

4. Anderson, M. W.; Barker, N. W., and Seldon, T. H.: A Clinical Evaluation of Powdered Human Blood Cells in the Treatment of Ulcers of the Extremities Associated with Vascular Disorders, Am. Heart J. **32**:754 (Sept. 27) 1946. Naide, M.: Treatment of Leg Ulcers with Blood and Concentrated Plasma, Am. J. M. Sc. **205**:489 (April) 1943. Heller, R. E.: The Pathology and Treatment of Indolent Ulcers of the Leg, Surg., Gynec. & Obst. **76**:77 (Jan.) 1943. Rees, H. C., and Slevin, J. G.: Surgical Management of Vascular Leg Ulcers, Surgery **21**:575 (April) 1947.

a considerable percentage of persons with ulcers of the legs. Pain in the ulcer is variable, but is probably more common with the ulcer due to arteriosclerosis than with the ulcer produced by stasis.

In differentiation of the ulcer of arteriosclerosis from stasis ulcers there are important negative findings. In almost all instances there are no, or minor, varicosities; there is seldom a history of thrombophlebitis or chronic cellulitis; edema is not often present, and deposits of hemosiderin are minimal or absent. There are seldom associated stasis changes or findings with the arteriosclerotic ulcer.

The accompanying table gives a brief résumé of 10 cases of ulceration associated with arteriosclerosis obliterans:

Observations in Ten Cases of Ulceration Associated with Arteriosclerosis Obliterans

Case No.	Age	Sex	Duration	Size (Cm.) and Location	Findings on Palpation of Pulses (Right/Left)			Oscillometric Readings (Right/Left)		Symptoms and Other Findings
					Popliteal	Posterior Tibial	Dorsalis Pedis	Thighs	Calves	
1	58	F	1½ yr.	2 by 3 Left anterior, lower third	0/0	0/0	0/0	2/1	1/0.5	Ulcer tender and painful to start; onset of pain in foot 5 mo. prior to entry Roentgenologic findings: Atrophy of bones of left
2 (Fig. 2)	61	F	5 yr.	5 by 5 Right lateral, lower third	0/+	0/0	0/0	Not done		Intermittent claudication; pain over ulcer; dependent rubor; nail changes
3 (Fig. 4)	76	F	8 mo.	10 by 18 Left posterior, middle third	?/0	0/0	0/0	Not done		Ulcer quite painful and very tender; numbness and tingling of legs for 2 wk.; nail changes
4 (Fig. 3)	76	M	2 yr.	6 by 12 Left medial, lower third	+/0	0/0	0/0	6/3	3.5/1.5	Temperature and color changes; shiny atrophy of skin of feet and legs
5	63	M	2 mo.	5 by 5 Right lateral, middle third	0/0	0/0	0/0	...	0.5/0.5	In 1944 typical arteriosclerotic gangrene of right great toe (amputated); temperature changes Roentgenologic findings: Atrophy of bone of fore
6	63	M	1½ yr.	5 by 9 Right anterior, middle third	0/0	0/0	0/0	0/10	0/5	Temperature and color changes; nail changes; scaling atrophy of skin of toes; intermittent claudication, left burning and tingling of both feet Roentgenologic findings: Atrophy of all bones of right foot and leg
7 (Fig. 1)	62	M	6 yr.	3 by 6 Right medial, malleolus	...	0/0	?/?	1/1.5	0.5/1	Intermittent claudication, "fanlike" aching pain from right midsole to inner aspect of thigh; numbness over lateral aspect of right knee leg; temperature and color changes; dry, scaling atrophy of skin of legs and
8	63	M	1½ yr.	2.5 by 4 Left posterior, medial malleolus	0/0	0/0	0/0	Not done		Temperature changes; scaling atrophy of skin of feet
9	67	M	38 yr.	2.5 by 10 Left medial, lower third	...	+/0	+/0	Not done		Temperature and color changes
10	68	M	3 mo.	6 by 9 Left medial, malleolus	sl/sl	0/0	0/0	2/.75	.75/.5	Shiny atrophy of skin feet; nail changes

SUMMARY OF CASES

Seven of the 10 patients with arteriosclerotic ulcers were male, and the average age for all was 65.7 years, the age group and sex incidence thus being that commonly found in arteriosclerosis obliterans. The duration of the ulceration varied widely, but except in case 9, in which severe stasis and arteriosclerosis obliterans coexisted, the average duration was about two years. For the remaining 42 patients in the total series, almost all of whom had stasis ulcers, the average age was 56.5 years; 55 per cent were female, and their ulcers had been present for an average duration of 8.5 years.

All surfaces of the lower leg and both malleoli were involved, and local descriptions varied greatly from those of deep, punched-out, dry

Fig. 1 (case 7).—The largest ulcer was located posterior and proximal to the right medial malleolus and measured 3 by 6 cm. in its greatest dimensions. The picture was taken after seven days of treatment, prior to grafting.

lesions covered with a thin, tenacious eschar to those of grossly purulent, foul ones with fair underlying granulations. Cultures of the ulcers taken on admission revealed a multiplicity of organisms, including the various streptococci and staphylococci and Proteus vulgaris, Pseudomonas aeruginosa, Proteus morganii, micrococci and diphtheroids, with no appreciable difference in this respect from the remainder of the ulcers in the series. It would appear that ulcers produced by arteriosclerosis obliterans have no significantly predominant location, appearance or contaminating organisms.

Two of the ulcers were definitely painful, the remainder exhibiting tenderness of varying degree, probably more pronounced than that in ulcers produced by stasis.

The diagnosis of arterial insufficiency was corroborated in each case by our repeated inability to palpate the posterior tibial, dorsalis pedis and popliteal arteries in the involved leg. Oscillometric readings, where performed, were greatly reduced in the extremity bearing the ulcer. In 4 of the cases, the uninvolved leg also gave decreased readings. Color changes were obvious in 5 cases and elicitable in the remainder. Decidedly decreased temperatures of the foot and leg were observed in 6 of the cases, and nail changes and atrophic dermatitis were each described in 6 cases. Roentgenologic evidence of osteoporosis was demonstrated in 3 of the cases.

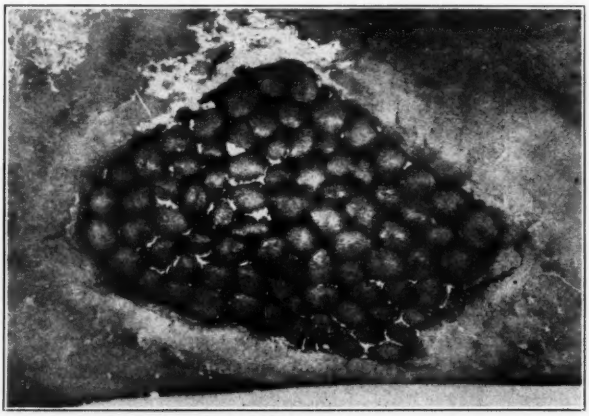

Fig. 2 (case 2).—The ulcer was located on the lateral surface of the lower third of the right leg and measured 5 by 5 cm. The picture was taken ten days after grafting, which was 100 per cent successful.

A definite history of intermittent claudication was obtained from 3 of the patients, and symptoms of numbness, tingling or pain, from 2 others. Most of the patients complained of coldness of the extremities.

The diagnosis of arteriosclerosis obliterans had been made two years previously for the patient in case 5, when there had occurred a typical arteriosclerotic gangrene of the right great toe which had necessitated amputation, but this person was the only one who had typical arteriosclerotic involvement of toes.

The differential diagnosis is concerned mainly with stasis ulcers, and these are almost always preceded by thrombophlebitis or large varicose veins, or both. Of the reported cases of arteriosclerotic ulcers, in only case 9, in which both conditions were present, was there a history of thrombophlebitis. Five years later, after ligation of the saphenous

vein, varicosities appeared. In 1 other case the patient had undergone ligation of the saphenous vein, although the patient was unaware of the prior presence of varicosities and had none on examination in this clinic.

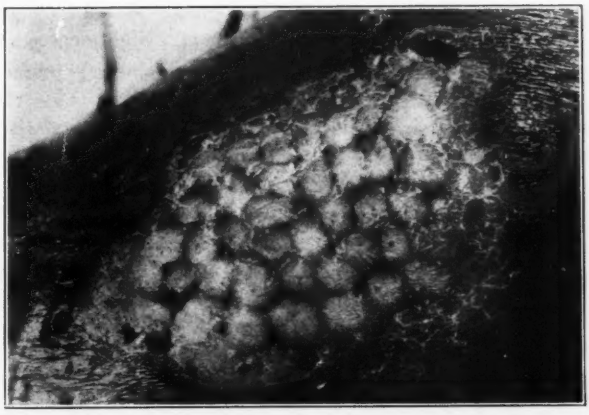

Fig. 3 (case 4).—The ulcer was located on the medial surface of the lower third of the left leg and measured 8 by 10 cm. The picture was taken four weeks after grafting, which was 100 per cent successful.

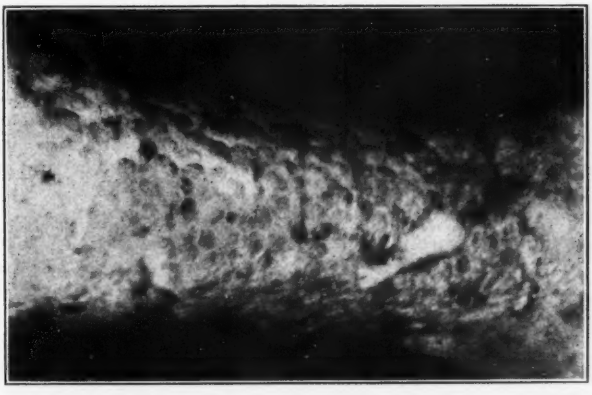

Fig. 4 (case 3).—This ulcer was the largest in the series, measuring 10 by 18 cm. and was located on the lateroposteromedial surface of the lower half of the left leg. The picture was taken thirty-six weeks after grafting and shows an excellent result.

In the remaining 8 cases, 3 patients presented mild varicosities which were insignificant as regards causation of the ulcers.

The stasis ulcer almost always occurs in a leg with severe edema and is usually surrounded by dermatitis and hemosiderosis. In 4 of the reported cases there was no appreciable edema, and in 5 others there was only mild dependent edema commensurate with that encountered in arteriosclerosis obliterans. In none of the cases was there significant dermatitis, and hemosiderosis, if present, was of a slight degree.

While stasis ulcers are commonly found on the medial surface of the lower one third of the leg, as were 50 per cent of the stasis ulcers in our series, the arteriosclerotic ulcers were located on all surfaces of the leg and about the malleoli, only 2 of the 10 involving the medial surface of the lower one third of the leg.

The appearance of the ulcer itself was often of little help. While some arteriosclerotic ulcers are ischemic in character, in most cases the appearance depends on the previous local treatment. Irritating and sensitizing applications have similar effects regardless of the cause of the ulcer. The size and shape of the ulcers also varied greatly, as do those of stasis ulcers.

In all the reported cases the patients had negative reactions to the Kolmer and Kline tests except in case 1, in which the patient had received adequate treatment without evidence of healing of the ulcer.

In none of the cases was there associated diabetes or polycythemia vera.

METHOD OF TREATMENT

In previous papers[1] from this clinic, the treatment of ulcers of the leg has been discussed. Treatment of the arteriosclerotic ulcer is almost as successful as the treatment of stasis ulcers. The following routine has worked very well in the treatment of these ulcers:

The patients are confined to bed rest but encouraged to move about the bed. The involved limb is maintained in a horizontal position. In the stasis ulcer, elevation of the limb above the horizontal in order to reduce congestion may be indicated, but in the arteriosclerotic ulcer elevation increases by means of gravity the resistance to an already decreased arterial supply.

Continuous application of dressings soaked in a one-half saturated solution of boric acid, at room temperature, are made to the ulcer. When Ps. aeruginosa is present, 0.25 per cent acetic acid solution is substituted. Externally applied heat is contraindicated in treatment of these ulcers.

When adequate granulations have developed, simple pinch grafting is done. A dry pressure dressing is applied to the grafted ulcer. Penicillin is administered intramuscularly for twenty-four hours prior to and forty-eight hours after grafting. After five days, the dry dressing is removed and wet dressings resumed until healing is complete. The patients are then gradually made ambulatory and instructed in the proper use of an elastic supportive bandage, usually incorporating a foam rubber sponge directly over the healed ulcer site. While these supportive measures find their primary use in stasis ulcers, they are of undoubted value in preventing recurrences of ulcers in arteriosclerosis obliterans, if only because of protection against trauma.

RESULTS OF TREATMENT

Treatment was successful in 9 of the 10 cases of arteriosclerotic ulcers. Three to fourteen days, with an average of 8.7 days, were required before the ulcers were ready for grafting. Cultures taken at the time of the graft revealed no growth in 3 cases, and combinations of hemolytic Staphylococcus aureus, Staphylococcus albus and diphtheroids in the rest. The primary take of the grafts varied from 92 per cent to 100 per cent, averaging 97 per cent. An average of 34.1 days after grafting was required for complete healing, with extremes of twenty-one and seventy-three days. The total period of hospitalization varied from twenty-eight to eighty-four days and averaged 42.8 days.

Of the remaining 42 patients in the series, all but 1 were successfully treated. They required an average of 8.3 days of treatment before grafting, and 29.3 days afterward for a total of 37.6 days of hospitalization, and primary takes averaged 88.7 per cent. It is seen that the results of treatment for the two types of ulcers were almost identical.

The failure of treatment for the arteriosclerotic ulcers occurred in case 6, in which a supracondylar amputation was eventually performed by the department of surgery. The popliteal artery was found to be completely occluded by atheromatous proliferation of the intima and thickening of the media. There was an associated chronic phlebitis with thrombosis, together with severe foreign body reaction of the popliteal vein.

Among the 9 patients successfully treated, there had been failures on the first attempt, with success on the second, in 2. In 1 of these the patient subsequently died of cerebral thrombosis.

The 8 living patients who were successfully treated have been observed for periods varying from eight to thirty-two months, without recurrence of their ulcers. The patient in case 5, the only one who presented typical lesions of arteriosclerotic gangrene in addition to the ulcer of the leg, returned to the surgical service twenty-one months later with progression of the arteriosclerosis obliterans, manifested by the development of a gangrenous lesion of the left great toe. The ulcer of the right leg which we had grafted remained healed.

COMMENT

Among the complications of arteriosclerosis obliterans, authors commonly include gangrene and ulceration of the toes, occasionally extending to the forefoot and, rarely, to the heel. Ulcers of the leg and ankle are mentioned only in passing, if at all. Exceptions are the descriptions of 2 cases by Samuels,[5] 2 cases associated with varicose

5. Samuels, S.: The Diagnosis and Treatment of Diseases of the Peripheral Arteries, New York, Oxford University Press, 1936, pp. 227-229; ed. 2, 1940, pp. 224-225.

veins by Verovitz,[6] and a group of 6 cases, 3 of which were associated with varicose veins, recently reported by Edwards.[7]

It appears that arteriosclerosis obliterans is primarily involved in the production of ulcers of the leg to a much higher degree than was previously thought.

While, as we have pointed out, the treatment of these ulcers differs little from that of the ordinary stasis ulcer, the importance of early diagnosis and treatment of the underlying arteriosclerosis obliterans should not be underestimated. In 9 of the 10 reported cases, the ulcer of the leg was the first manifestation of the disease.

SUMMARY

Ten of 52 cases of chronic ulcers of the leg were thought to have been caused wholly or in part by arteriosclerosis obliterans.

The ulcers produced by arteriosclerosis obliterans occurred oftener in males of an older age group and were of shorter average duration than the rest of the ulcers in the series.

The appearance and location of these ulcers were not distinctive.

Symptoms of numbness, coldness or tingling were usually present, and sometimes there was a frank history of intermittent claudication. Objective findings of impaired arterial circulation were present in all 10 cases.

History or evidence of thrombophlebitis, varicosities, severe edema, dermatitis and hemosiderosis, which, if present, would indicate chronic venous insufficiency, was almost entirely absent.

Treatment, utilizing pinch skin grafts, was successful in 9 out of 10 cases.

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6. Verovitz, C. H.: Diseases of the Veins and Lymphatics of the Lower Extremity, Boston, The Christopher Publishing House, 1941, pp. 219-221.

7. Edwards, E. A.: Necrotic Lesions of the Leg in Arteriosclerosis, New England J. Med. **239**:571 (Oct. 14) 1948.

PARAKERATOSIS SCUTULARIS (OSTRACEA)

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THE CASE about to be reported is of one of those very rare anomalies which fall under the title of parakeratosis scutularis (ostracea), a name contributed to dermatology by Unna in 1890.[1]

REPORT OF A CASE

History.—S. McL., a Scotsman aged 66, appeared at a clinic of St. John's Hospital for Diseases of the Skin in the summer of 1948. He stated that thirty-four years ago a scaly rash had developed on the elbows, the backs of the forearms and the anterior aspect of the lower limbs from the middle third of the thighs to the ankles. Heaped-up lesions began to appear on these sites within six months. After an interval of approximately five years, some lesions resolved, leaving scars. There had never been any subjective symptoms. The patient had tried innumerable local applications, without benefit. The only medicine he had taken internally was acetylsalicylic acid.

He could recollect no cutaneous disease of any kind in any of his relatives. He had no offspring. He had had a particularly healthy life; he had never been beyond the shores of the British Isles. His occupation had always been that of a house decorator.

Examination.—The patient was a well built, tall man. No abnormality was found on general systemic examination. The hair, nails and mouth were normal. The lesions were situated on the anterior surfaces of the legs, on the areas described previously, as well as on the backs of the elbows. They consisted primarily of heaped-up, laminated, yellowish masses, not dissimilar to an oyster shell. They varied in size from a ¼ inch to ½ inch (0.6 to 0.2 cm.) in diameter. There was no surrounding erythema. The edges of the masses were thinner, and were attached to the skin, as if suction had been used for their adherence. They were not easily detachable. When detachment was done, no bleeding occurred, but the denuded under surface showed some thornlike horny balls, of the sort which Unna was the first to observe. Deep scars were also present, in some cases adjacent to, and in others separate from, the heaped-up keratotic masses. The surface of the scars varied in consistency; the peripheral margins were for the most part obviously undermined and reflected the extent to which the horny shell had penetrated. Over the normal skin of both legs in their lower two thirds, deep brown pigmentation was present (fig. 1).

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1. Unna, P. G.: Parakeratosis Scutularis, in Internationler Atlas von seltener Hautkrankheiten, Hamburg, L. Voss, 1890.

These lesions were mainly distributed over the lower limbs. Those of the elbows were considerably fewer. Apart from the form of lesion previously described, the elbows showed several plaques, an inch (2.5 cm.) in diameter, raised and covered with silvery scales, a picture rather suggestive of psoriasis.

Laboratory Investigations.—The Wassermann and Kahn reactions of the blood were negative on three occasions, and the red and white blood cell counts were normal.

Fig. 1.—Clinical appearance of patient's legs, showing heaped-up, laminated lesions, deep scars and deep pigmentation.

Histologic Picture (Dr. Henry Haber).—The epidermis showed pronounced parakeratosis, several times the thickness of the normal skin. It was arranged in whorls, containing well defined nucleated cells, as well as several microabscesses, between the layers. In some places, there was a solid hyperkeratosis extending deeply into some very dilated follicles. Irregular acanthosis was present, with intercellular and intracellular edema and immigration of polymorphonuclear leuko-

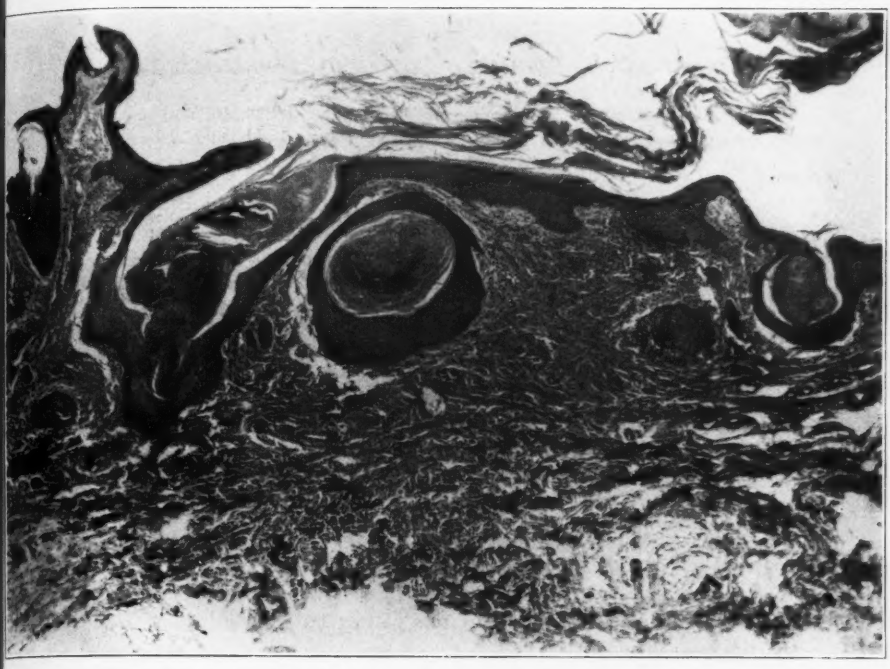

Fig. 2.—A section of epidermis, showing pronounced parakeratosis in whorl formation.

Fig. 3.—A view, under higher magnification, of a portion of the field shown in figure 2.

cytes. The upper third of the corium exhibited edema, vascular dilatation and a diffuse inflammatory reaction consisting of lymphocytes, endothelial cells and a few giant cells.

COMMENT

Apart from the original case described by Unna, the only one to be found in the literature was that of Weiss, reported in 1912.[2]

The symptoms of this case correspond in most instances to those in the original description, the lesions being essentially the same and presenting the curious cupping, cuplike adherence to the skin. The sites affected were, however, different. In the original case, the skin involved was that on the scalp, the upper parts of the thighs and arms and the sacral region, as well as the finger nails. This patient had no disorder of the scalp or nails, but the striking anomaly in the form of the peculiar scarring had hitherto not been noted. The cases of Unna and Weiss were in younger people (respectively, a man aged 41 and a girl aged 18); the patients were examined at the onset of the disease and, as far as can be ascertained, were not reviewed in later years. It may possibly be presumed that scarring did then develop. I was more fortunate in that I saw this patient late in the history, when scarring was pronounced.

The pathologic picture in the present case confirmed the findings in the 2 previously recorded cases. As in Weiss's case the evidence in the corium for chronic low grade inflammation was particularly notable.

Various forms of empiric treatment were employed without success. They included application of ichthammol (ichthyol®) and tar pastes and mixtures of potassium iodide and potassium arsenite solution (liquor arsenicalis). A preparation containing vitamin A was also tried over a six week period, in a dosage of 33,000 units thrice daily.

The clinical picture of this disorder is so wholly unlike any other in the realm of dermatology that differential diagnosis is extremely limited. Rupial syphilis can be readily excluded by appropriate investigation. At first glance, the casual observer might make the suggestion of psoriasis, but psoriasis does not form heaped-up keratotic masses, and the psoriatic lesion bleeds on scratching.

Several observers have expressed the opinion that parakeratosis scutularis is a rare and unusual form of psoriasis. I do not subscribe to this view. Parakeratosis scutularis is very different from the rupial variety of psoriasis, clinically and histologically: the recognized unorthodox varieties of psoriasis have been legitimately classified under the single heading because if at least the clinical picture was dissimilar, the pathologic one was basically identical.

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2. Weiss, L.: Parakeratosis Ostracea, J. A. M. A. **59**:343 (Aug. 3) 1912.

Neither in this case of parakeratosis scutularis nor in that of Weiss is there any microscopic resemblance of the lesions to those seen in psoriasis. This disease is at present a separate unknown entity. It is not justifiable to associate it with the group over which psoriasis is guardian; all one can truthfully say is that it is one of the parakeratoses and only in that respect a relation of psoriasis.

Permission to publish the case report was granted by Dr. A. Porter, and the photograph of the patient's legs was supplied by St. John's Hospital for Diseases of the Skin.

42 Fitzwilliams Square.

INVESTIGATION OF FUNGI IN HANGING DROP CULTURES

Preliminary Report

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AND
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THE METHOD of systematic observation in the hanging drop is widely used and has been universally accepted for detailed microscopic study of the morphologic structure and development of fungus cultures.

The technic of inoculation into the hanging drop is simple and well known: A drop of liquid medium (sugar broth or beer mash) is placed in the center of a cover slip under sterile conditions, and a small portion of the test culture is introduced into the thick of this drop; the culture must be grown in solid or liquid mediums in a test tube or in a big tube. The cover slip is next covered with a slide having a depression in its middle portion so that the center of the depression lies over the drop. The edges of the depression are smeared with petrolatum in order to fix the cover slip to the slide.

The specimen, a microsubculture, thus obtained allows a systematic study of the morphologic features of the fungus culture—its growth and development under the microscope. This method has proved of great help in everyday practice in investigation of cultures grown in solid mediums, in cases in which the gross appearance as well as the microscopic picture of small portions of cultures did not yield enough data for exact determination of the species to which they belonged.

The method of investigating fungus cultures in the hanging drop as it is now usually practiced demands previous cultivation of native pathologic material in solid or liquid medium in a test tube. Hence the microculture in the hanging drop is really a subculture.

The process of development of the subculture in the hanging drop must necessarily depend on the nature of the fungus and the amount sown—the number of organisms being arbitrary. Consequently, it

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From the Ukrainian Institute of Dermatology and Venerology (Director, Prof. A. M. Krichevsky).

Read before the Section on Dermatology and Venerology of the Medical Association of Charkov, July 13, 1946.

must differ according to the elements prevailing in the subculture, the age of these elements and their capacity for continued growth and development.

The variations often seen in the growth of fungus subcultures in the hanging drop and the lack of growth not infrequently observed may be partially accounted for by these circumstances.

Another important drawback in the study of the morphology of subcultures in the hanging drop is the fact that this method gives no possibility of observing the culture while it consists of individual fungus elements of the original pathologic material.

Moreover, the method of studying subcultures in the hanging drop naturally causes a certain delay in the process of investigation, and identification of the fungus is thus postponed for at least the lapse of time necessary to obtain the initial culture in a test tube or other tube. It is well known that this lapse of time is identical neither for the various species nor for fungi under different conditions; sometimes a fortnight or more is required for this end. This drawback induced us to search for a means of identifying microcultures of fungi in the hanging drop, not in subculture but in the first generation obtained by inoculating original pathologic material into a hanging drop. This method has been proposed by one of us (S. M. Rafalovich).

The technic of inoculation and preparation of a specimen of microculture from native material is the same as that which is in common use for preparing the hanging drop, with the difference, however, that a small piece of the native pathologic material instead of a portion of the culture is inoculated into the hanging drop.

We used a small piece of hair which we had first examined microscopically to ascertain the presence of fungi. This hair was introduced into a drop of beer mash [1] by means of a sterile loop, as previously described.

We left the specimens thus prepared at room temperature or placed them in an incubator at 24 to 28 C. and examined them daily to follow the development of the culture.

The first experiments proved that such specimens allow one to follow under the microscope the gradual growth and development of the microculture in the hanging drop for several months from the time when it first forms from the fungus elements in the original material to its complete development and maturity.

The growth of a culture obtained from native material usually begins on the second, third or fourth day following inoculation, starting either

1. Beer mash (350 cc.) filtered through cotton wool was diluted with 650 cc. of distilled water. The mixture was sterilized at 110 C. for ten minutes in an autoclave; the medium was then filtered again, poured into sterile test tubes and sterilized once more at 110 C. for ten minutes.

at one pole of the hair or appearing almost simultaneously at both ends and all over its surface. The growth takes the appearance of a comparatively large number of mycelium threads which spread like radii in all directions from the inoculated bit of hair (fig. 1).

By observing the growth and development of the microculture in the hanging drop, one may witness a series of features typical for the species, insuring the recognition of the growth without the need of inoculation of these cultures into test tubes.

Up to now our observations have been made on the kind of fungi most commonly met with in our practical work—Trichophyton violaceum, Trichophyton crateriforme, Trichophyton gypseum, Microsporon lanosum and Achorion schönleini. So far we have followed in the hanging drop 58 specimens of native material, Tr. violaceum being represented by 14 specimens (18 inoculations); Tr. crateriforme by 5 (9 inoculations), Tr. gypseum by 6 (14 inoculations), M. lanosum by 5 (9 inoculations) and A. schönleini by 6 (8 inoculations).

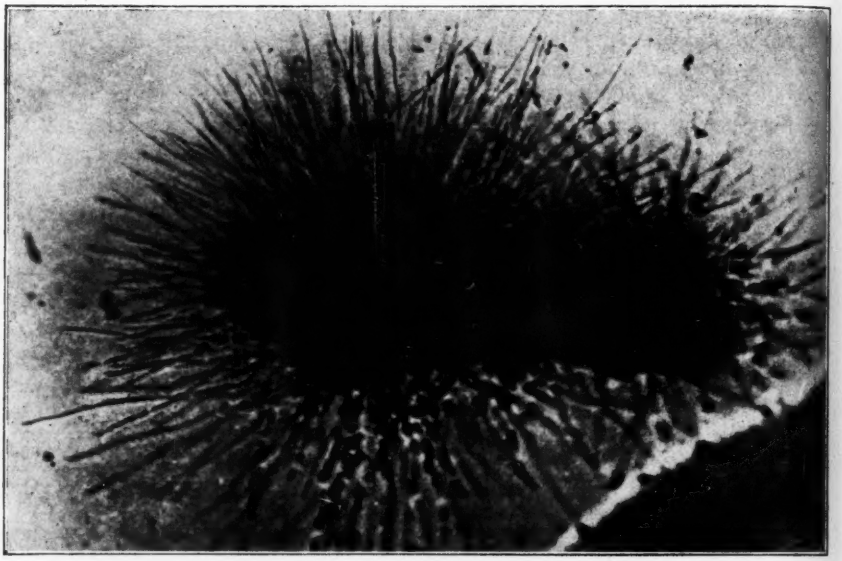

Fig. 1.—Mycelium threads issuing radially from an inoculated piece of hair (four days after inoculation).

OBSERVATIONS

Tr. violaceum.—In the hanging drop the microculture usually begins to grow on the third or fourth day after inoculation, its identification becoming possible from the sixth or seventh day on.

During the period of development the culture consists of a short freely branching mycelium. This mycelium is of medium thickness, tapering toward the ends, with more or less rare septums, containing solitary spores along its length. The mycelium does not manifest any tendency toward fast centripetal growth and continues chiefly to be confined to the vicinity of the inoculated bit of hair, bearing a certain resemblance to a heap of dead brushwood (fig. 2).

These features proved quite sufficient to identify the culture on the sixth or seventh day after inoculation. On the tenth or twelfth day a considerable amount of intercalated and a few terminal chlamydospores were observed in the microculture. Later, the number of chlamydo-

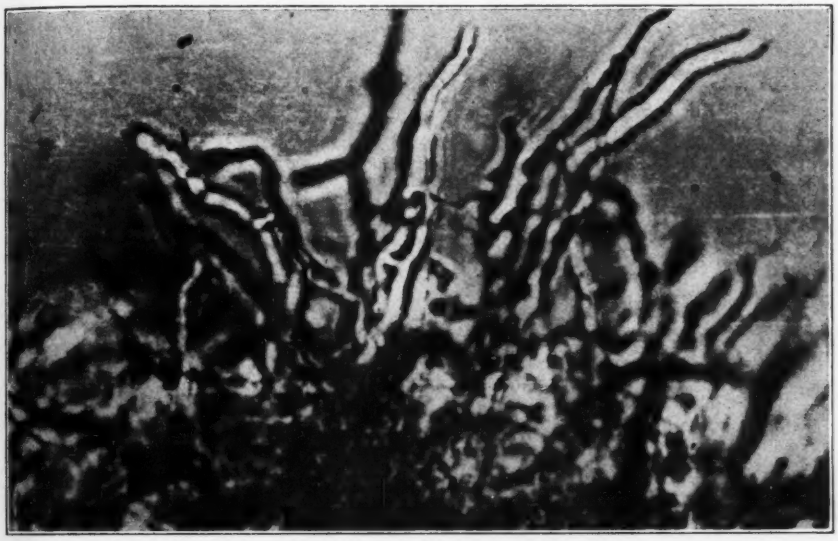

Fig. 2.—Tr. violaceum; short mycelium, scantily septate, with a few spores along its course (tenth day after inoculation).

spores increases so that at the end of two or three months they fill the specimen completely (fig. 3).

According to the observations of Bruns and Alexander, growth of a culture of Tr. violaceum proceeds very slowly. Podwysotzkaya and Kashkin have observed growth seven, eight, ten and twelve days after inoculation, depending on the surrounding temperature.

Our personal observations have also confirmed the slow growth of this culture in the solid medium of Sabouraud and have, moreover, shown that this kind of fungus is often hard to recognize because it is scanty in the microscopic picture owing to the late date at which the culture takes a violet color.

Tr. crateriforme.—The growth of the microculture obtained in the hanging drop from native material began in 7 experiments on the third or fourth day after inoculation. In 1 instance growth was first observed on the eighth day, and in others it was lacking; in both these instances the temperature at which the drops were kept was unfavorable for the development of the culture.

On the first day that growth of Tr. crateriforme microculture became visible, it consisted of straight mycelium threads of medium thickness, longer than those of Tr. violaceum; part of the mycelium was septate (the septums being few), and the mycelium itself issued from all sides of the bit of hair, spreading toward the edges of the hanging drop.

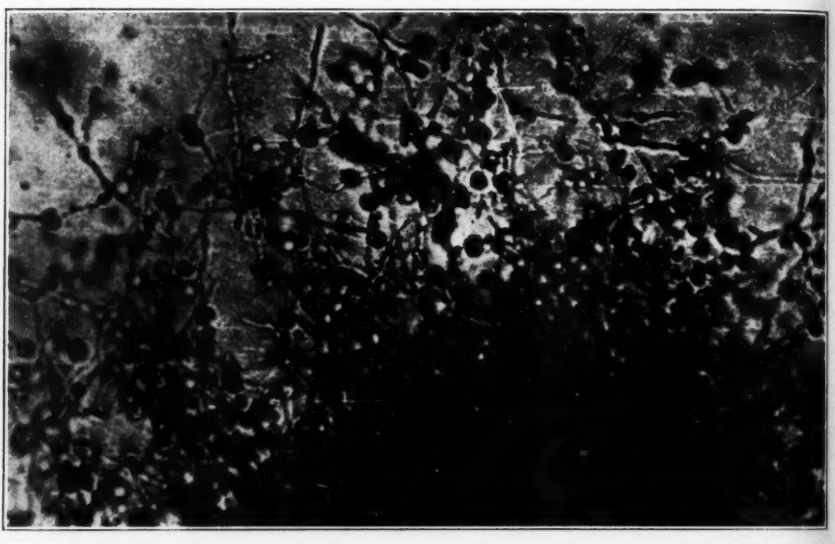

Fig. 3.—Tr. violaceum; numerous chlamydospores (four month old culture).

All along its length the mycelium had short branches (hyphae), part of which resembled rudimentary spindles owing to thickening of the protoplasm. Moreover, the same specimens showed comparatively numerous plainly visible spindles with three, five, six or sometimes even ten septums, arising from the ends of the mycelium or from its branches. Sometimes the spindles appeared one or two days later.

Spindle formation in the microculture allows one to identify a trichophyton producing an endothrix infection, such as Tr. crateriforme, as early as the first day of growth (fig. 4). Six or seven days after inoculation aleurae appear in the microculture; at the same time some terminal and intercalated chlamydospores become visible. At a later date, when the culture is aging, the mycelium pales but its silhouette

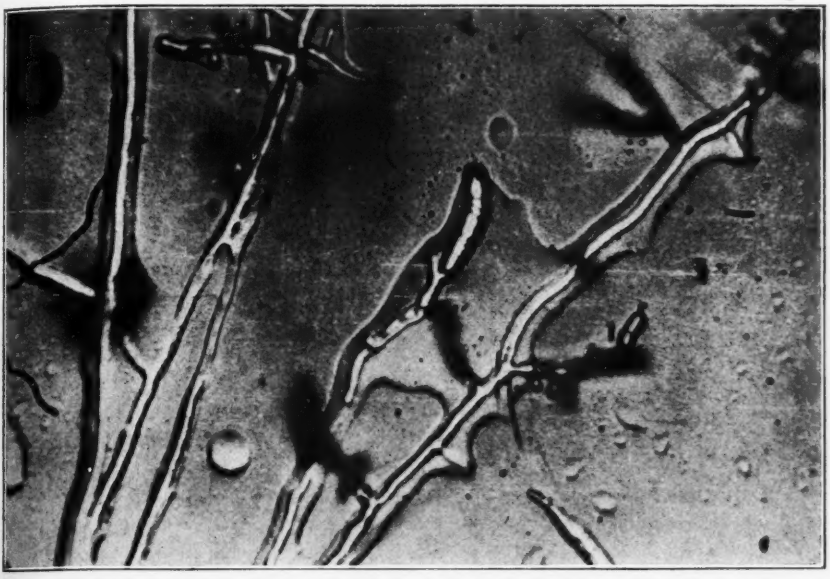

Fig. 4.—Tr. crateriforme; long mycelium with short branches, side conidia and a spindle with 3 chambers (seventh day after inoculation).

Fig. 5.—Tr. crateriforme; numerous spindles (three month old culture).

remains visible, with agglomerations of protoplasm in the shape of longitudinal chains and with spindles and side conidia (fig. 5).

We consider it of interest to stress the point that spindles were always found when Tr. crateriforme was cultivated from native material in a hanging drop of beer mash, whereas we have never observed them when we were investigating microscopically small portions of cultures taken from solid mediums, nor had any been present in microsubcultures when specimens from solid mediums were introduced into a hanging drop. This is all the more interesting from the fact that in the table of botanical classification of dermatophytes of Grikoraki and Guyard (constructed in accordance with the characteristics of the organs of reproduction) the culture of Tr. crateriforme has been placed into the group of chlamydoaleurosporia and not into that of claustroaleurosporia.

In the literature accessible to us we did not find mention of the presence of spindles with two or three open spaces in them or of rudiments of such structures in a culture of Tr. crateriforme in any work except an article of Gavrilova (from the Institute of Dermatology and Venerology of Leningrad). Gavrilova stated, however, that he had studied a vast number of cultures of various strains of this fungus with a view of finding spindles and had observed only a very few.

Our observations on the growth of Tr. crateriforme in the hanging drop allow us to assume that spindles appear under certain conditions, forming, as a rule, one of the earliest signs for the recognition of these cultures. It must be said here that in one instance when we expected to obtain spindles in the hanging drops, in view of the results of control inoculations of solid medium, we were unable to see any, despite repeated inoculations. We therefore inoculated a solid medium (agar with beer mash) in a large tube; this culture lacked crater formations. Evidently it did not belong to Tr. crateriforme but to one of its satellites.

Tr. gypseum.—Among the 14 cultures of this fungus the growth of the microculture was observed five times on the second day, five times on the third and once on the fourth day after inoculation. In 3 cultures there was no growth; the culture had been kept at a low temperature in 2 of these instances.

On the first day of growth the culture consisted of long mycelium threads bearing more or less short branches (hyphae) with a few spores along them. The branches were at various distances from each other. On the following day—that is, on the third or fourth day after inoculation—the microculture contained a considerable number of blunt-pointed long spindles; the number of chambers in them reached ten. The microscopic picture here described permits recognition of the culture as belonging to Tr. gypseum on the third or fourth day after inoculation (fig. 6). At the end of the second week, and sometimes even earlier, numerous coils and spirals appeared in the specimen (fig. 7).

Fig. 6.—Tr. gypseum; blunt-ended long spindles and aleura (three day old culture).

Fig. 7.—Tr. gypseum; spirals and coils and agglomerations of aleura (seven day old culture).

It must be said that when one is investigating a portion of Tr. gypseum culture obtained in the usual way in solid medium, it is often difficult to discover the spindles and spirals because of the fact that the spores are sometimes so numerous that they hide the mycelian structure of the cultures. In order to study the culture with more details it became necessary to consider the peripheral zone of the specimen, where the spores are not so numerous, or to make use of subcultures in a hanging drop, which requires more time.

Microsporon lanosum.—Seven of the 9 cultures kept thermostatically at the usual room temperature showed growth on the third day, whereas 2 specimens cultivated at a lower temperature did not produce

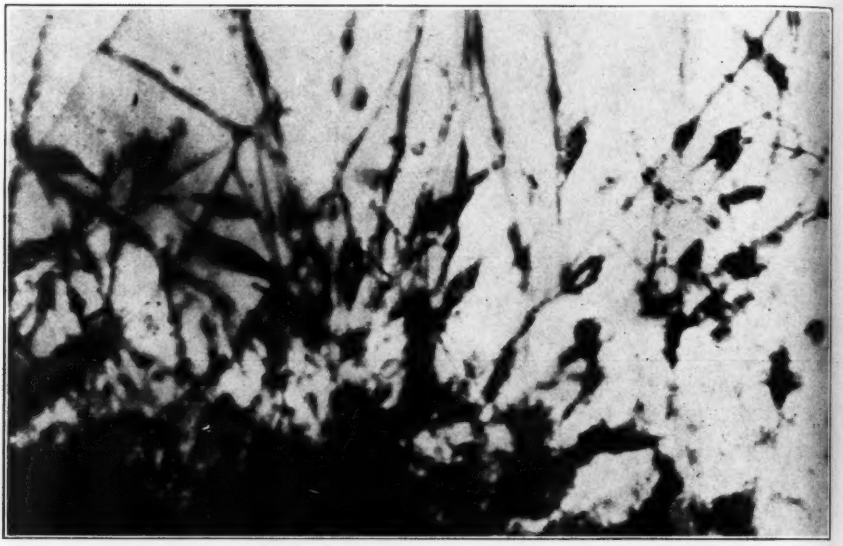

Fig. 8.—M. lanosum; spindles and bamboo-like stems, (six days after inoculation).

growth until the sixth day. One the first day of growth the microcultures consisted of a long or slightly curving mycelium, slightly tapering at the ends, with short branches. The septums were few in that mycelium. The protoplasm was not distributed uniformly; sometimes it took the shape of rosaries or chains, whereas in other cases the protoplasm contained thickened parts all along the mycelium or in its branches; some rudimentary spindles also were present. Single sessile spores, side conidia and crest-shaped organs became visible. On the third day of visible growth—that is, usually on the sixth day following inoculation—spindles typical for M. lanosum made their appearance and the culture could be perfectly well identified (fig. 8).

In the course of the following months the growth of the culture proceeded without any significant alterations. The mycelium had outgrown the limits of the drop, carrying the medium along with it. In some instances the microcultures were kept under observation as long as four months, and when we had transferred them to solid mediums we found that they yielded growth.

A. Schönleini.—General growth of the culture becomes visible on the second or third day after inoculation. On the first day of growth straight and curved threads of mycelium with branches were observed microscopically, issuing from the bit of hair inoculated; these threads

Fig. 9.—A. schönleini; club-shaped thickenings, solitary intercalated chlamydospores; characteristic thickened branching (seven day old culture).

of mycelium were of irregular thickness, with some rare spores on them. The ends of the mycelium were thin and rounded and looked as if they had been chopped off. Part of them had characteristic dicotomous short and thickened branches or they were inflated (club shaped). Single big terminal or intercalated chlamydospores were seen. On the third or fourth day of growth the number of club-shaped inflated forms increased, crest-shaped organs, stag's antlers and candelabras making their appearance.

The microscopic picture here described usually permits one to identify a culture of A. schönleini on the third or fourth day after inoculation (fig. 9).

CONCLUSIONS

The few observations made by us of the growth and development of microcultures from native pathologic material (hair infected with fungi) examined in a hanging drop of beer mash warrants the following preliminary conclusions.

1. The method of inoculating native pathologic material into a hanging drop of nutritive medium (beer mash) is suitable for the study and identification of fungi invading hair.

2. The method is simple and convenient and may easily be used in any laboratory.

3. The advantages of this method consist in the possibility of following the development of a microculture in a hanging drop during the stage of initial generation of native material.

4. Observations of microcultures of Tr. crateriforme in a hanging drop show the organs of reproduction to be septate spindles, typical for the culture of this fungus: this fact allows one to consider Tr. crateriforme as being a member of Tr. closteroaleurosporia.

5. In many instances the method here proposed saves time for identification of the fungus; this fact may be of value from the point of view of epidemiology.

Clinical Notes

SEBACEOUS NEVUS AND NEVUS SYRINGOADENOMATOSUS PAPILLIFERUS OCCURRING AS A MIXED FORM

Report of a Case

MORRIS D. MARCUS, M.D.
ST. LOUIS
AND
WILFRED E. WOOLDRIDGE, M.D.
SPRINGFIELD, MO.

Mixed nevi are not uncommon. Perhaps the most frequent types are vascular, such as the hemolymphangioma. Sebaceous nevi in which apocrine glands occurred have been reported by Robinson [1] and Koch,[2] and Koch [2] stated that eccrine glands have also been noted in these nevi. It should be emphasized, however, that the apocrine and eccrine elements, when they have occurred, have seemed to be normal and entirely independent of the nevus. Sachs and Lewis [3] reported a case which showed a mixed tumor containing cartilage and bone, in the deep part of which a nevus syringoadenomatosus papilliferus was present.

To find a nevus consisting of two entirely distinct congenital malformations, each of them rare in its own right, is most unusual. For this reason we report a mixed nevus of a type not heretofore described in the literature, one consisting of a sebaceous nevus and a nevus syringoadenomatosus papilliferus.

REPORT OF CASE

P. G., a girl 8 years of age, was first seen by us in the dermatology clinic of the Barnard Free Skin and Cancer Hospital. Her complaint was of a lesion on the left cheek which had been present since birth (fig. 1). The lesion had never changed in appearance until the child was 4 years of age, at which time her local physician had electrodesiccated its upper pole. Since that time the treated portion of the lesion had constantly discharged a small amount of milky fluid.

On examination it was noted that the left cheek was slightly fuller than the right. Over this area there was a lesion which measured 27 by 10 mm. This lesion was slightly raised and presented a soft, verrucous, light yellow surface, and a number of prominent follicles were noted within its borders. At the superior pole of the lesion was a bright red, moist papule from which drained a small amount of opalescent fluid. No definite ulcer could be made out, and the fluid seemed to ooze from the surface of the papule. The lesion was not tender.

Studies, observations and reports from the Dermatological Departments of the Barnard Free Skin and Cancer Hospital and the Washington University School of Medicine, St. Louis, service of Richard S. Weiss, M.D.

1. Robinson, S. S.: Sebaceous Nevus (Jadassohn): Report of Four Cases, Arch. Dermat. & Syph. **26**: 663-670 (Oct.) 1932.

2. Koch, F.: Ueber Vorkommen von apokrinen Drüsen in Talgdrüsennaevi, Arch. f. Dermat. u. Syph. **174**: 126-131, 1936.

3. Sachs, W., and Lewis, G. M.: Naevus Syringadenomatosus Papilliferus (Werther): Report of Five Cases, Arch. Dermat. & Syph. **36**: 1202-1209 (Dec.) 1937.

No other abnormalities were noted. Diagnoses of lymphangioma and sebaceous nevus were considered. The patient was referred to the surgical clinic, where a knife excision and suture were performed, with good cosmetic result, by Dr. Warren Smith.

Fig. 1.—Photograph showing lesion on left cheek.

Fig. 2.—Strip photograph showing (*A*) nevus syringoadenomatosus papilliferus and (*B*) areas of sebaceous nevus; × 10.

Histologic Report.—Most of the tissue was composed of closely packed sebaceous glands (figs. 2 and 3), some of which were abnormally placed immediately beneath the epidermis. Part of the glands opened into follicles. An inflammatory mixture of round cells and plasma cells was interspersed between the glands.

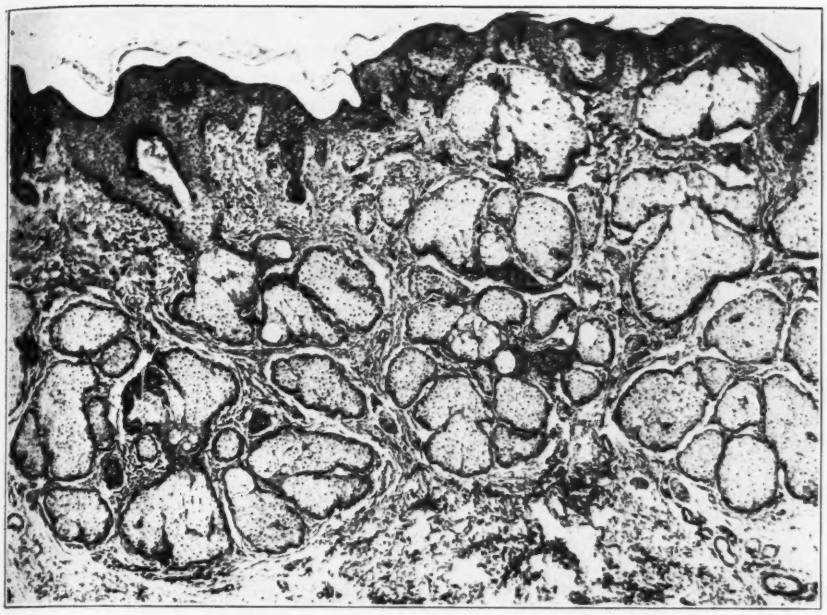

Fig. 3.—Photomicrograph showing sebaceous nevus; × 58.

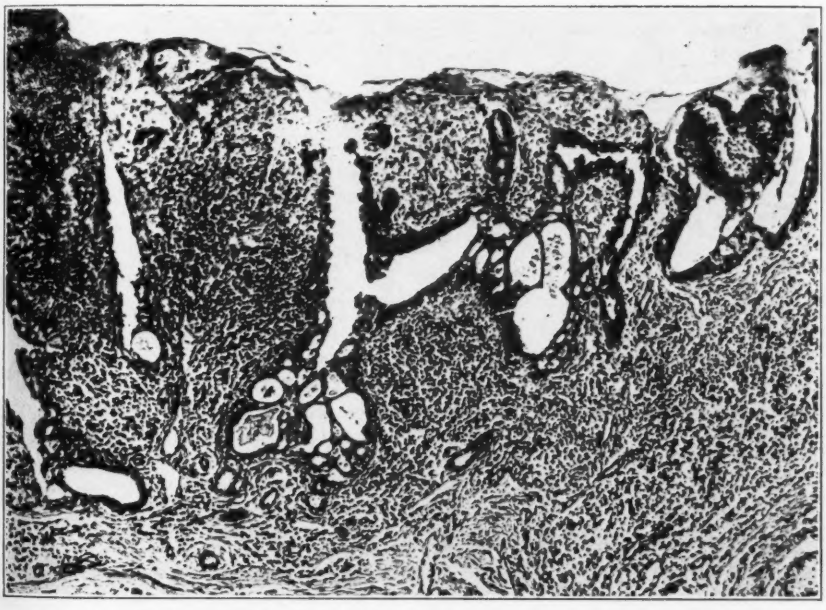

Fig. 4.—Photomicrograph showing nevus syringoadenomatosus papilliferus; × 88.

Fibrosis was present and followed the framework of the glands. A different type of tissue, composed of sweat gland elements, was present toward the edge of the section (fig. 4). These glands were dilated, tortuous and cystic and communicated with the surface of the skin. The cysts were lined with two layers of cells, the inner being cuboidal, and the outer, more elongated and columnar. Projecting into the lumens were many epithelial processes. A dense inflammatory infiltrate of round and plasma cells was seen between the glands. A connective tissue framework supported the sacs.

SUMMARY

A case of a mixed nevus which contained two distinct types of structures, a sebaceous nevus and a nevus syringoadenomatosus papilliferus, is reported. Each form occurs infrequently, and it is all the more unusual that both should occur within the same lesion.

GRANULOMA PAPULONECROTICUM OR PAPULONECROTIC TUBERCULID

Report of a Case

WILLIAM GUY Jr., M.D.
PITTSBURGH

Macleod and Ormsby,[1] Leiner and Spieler,[2] Whitfield,[3] Gougerot and Laroche [4] and others reported finding tubercle bacilli in lesions of papulonecrotic tuberculid, as determined by both animal inoculation and study of slides. Pollitzer,[5] Brault,[6] Gaucher,[7] Messa,[8] Ledo,[9] MacKee[10] Elliott,[11] Guy [12] and many other careful investigators presented evidence against tuberculosis as the cause of the condition. Opinions of contemporary writers are quite as confusing as those of the aforementioned authors. It would seem advisable to adopt the term granuloma papulonecroticum, as suggested by Pollitzer, because it becomes apparent that the clinical picture may occur as a tuberculous manifestation or independently of tuberculosis.

From the Department of Dermatology and Syphilology, University of Pittsburgh.

1. Macleod, J. M., and Ormsby, O. S.: Brit. J. Dermat. **13**:367, 1901.
2. Leiner, C., and Spieler: Wien. med. Wchnschr. **59**:1041, 1909.
3. Whitfield, cited by Ormsby, O. S.: A Practical Treatise on Diseases of the Skin, ed. 2, Philadelphia, Lea & Febiger, 1921, p. 692.
4. Gougerot, H., and Laroche, G.: Arch. de méd. expér. et d'anat. path. **20**:581, 1908.
5. Pollitzer, S.: J. Cutan. & Genito-Urin. Dis. **10**:9, 1892.
6. Brault, J.: Bull. Soc. franç. de dermat. et syph. **17**:40, 1906.
7. Gaucher, Louste and Christen: Bull. Soc. franç. de dermat. et syph. **20**:170, 1909.
8. Messa, F.: Riv. di clin. pediat. **8**:586, 1910.
9. Ledo, A.: Rev. de med. y cirug. práct. **88**:54, 1910.
10. MacKee: J. Cutan. Dis. **31**:568, 1913.
11. Elliott, J. A.: J. Michigan M. Soc. **16**:22, 1917.
12. Guy, W. H.: Etiology of Papulonecrotic Tuberculid, Arch. Dermat. & Syph. **8**:754 (Dec.) 1923.

The following case is reported because of findings contrary to the tuberculous theory of its genesis and an apparent cure resulting from the intracutaneous administration of a bacterial antigen.

REPORT OF CASE

A man, 24 years of age, whose previous medical history was irrelevant, presented an eruption of ten years' duration. Lesions were present on the arms and

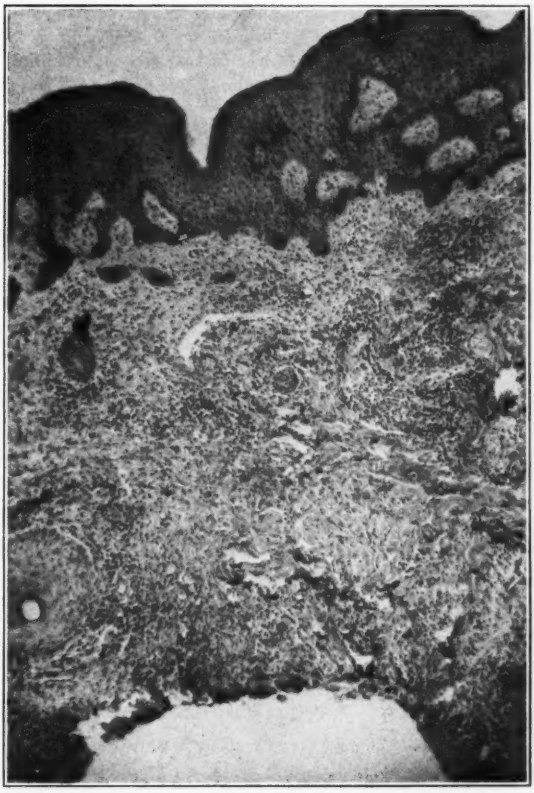

Fig. 1.—Lower power magnification of histologic section of active lesion.

legs. Indolent, subjectively asymptomatic papules became centrally necrotic and finally healed, leaving characteristic scars. Lesions appeared in crops, and the general health was not affected. The patient, an electrician (overweight, weighing 236 pounds with a height of 5 ft. 8 in.), enjoyed the best of health except for an actinomycosis that developed during the presence of the eruption and cleared promptly under treatment with iodides and roentgen rays. During the course of the disease, various types of therapy were tried, with indifferent results: the intra-

venous administration of arsenical compounds helped but produced neither complete nor permanent cure. The same could be said for treatment with roentgen radiation and various local applications, for example.

In January 1947 a complete survey was made, including a physical examination, a stereoscopic roentgenogram of the chest and laboratory studies; the last mentioned included a complete blood count with differential count, determination of the sedimentation rate, analysis of blood chemistry, glucose tolerance test, determinations of blood calcium and cholesterol, tests for hepatic function, determinations of the basal metabolic rate, Wassermann and Kahn tests, gastric analysis, urinalysis, testing for renal function, examination of stools, smears and cultures from lesions, histologic examination, experiments with inoculation, tests for sensitization to food, tests with bacterial antigen and a tuberculin test. Smears and cultures showed

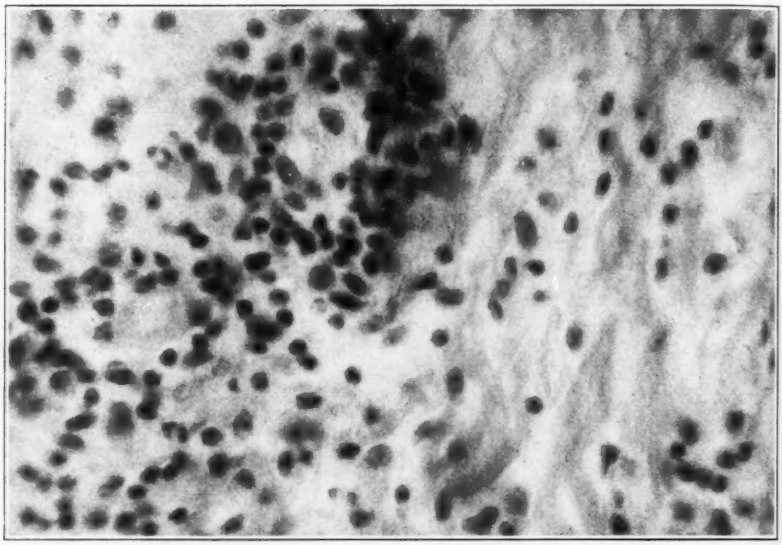

Fig. 2.—High power magnification of histologic section, showing tuberculoid structure.

Staphylococcus albus and Staphylococcus citreus. Experiments with inoculation had no significant results nor did the others, except as follows: Direct smears of stools showed an overwhelming predominance of staphylococci, with very few gram-negative bacilli and only occasional Escherichia coli and Clostridium perfringens organisms. Of the bacterial antigens, that of Esch. coli gave a 4 plus reaction by intradermal test. Other bacterial antigens elicited negative reactions.

On the strength of the aforementioned observations I decided to try desensitization by the administration of undenatured bacterial colon bacillus antigen. After failure with hypodermic injections in ascending doses, intracutaneous injections were begun at 0.1 cc. and increased by 0.1 cc. weekly up to 0.5 cc. This treatment led to complete disappearance of active lesions in three months, and there has been no recurrence to the time of writing (six months later).

SUMMARY AND CONCLUSIONS

1. Contrasting opinions on etiology are cited.

2. In view of the failure to demonstrate tuberculosis in all cases it is suggested that granuloma papulonecroticum is the preferable term for the disorder.

3. A report is made of a long-standing case, in which no tuberculosis was found, but in which a very strong sensitivity to Esch. coli was demonstrated and in which intradermal administration of an undenatured colon bacilli-antigen produced an apparent cure.

7026 Jenkins Arcade (22).

DERMATITIS CAUSED BY GARLIC

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JOHNSTOWN, PA.

The literature abounds with reports of unusual cases of contact dermatitis. I have recently observed a case which I think deserves mention.

R. V., a 56 year old man, presented himself on account of a scaly vesiculo-erythematous eruption measuring 4½ by 2½ inches (11 by 6 cm.), located on the lateral aspect of the left forearm above the wrist. The patch had poorly defined borders and was pruritic. The patient had worked in a meat-packing plant as a meat grinder for twenty-seven years and had had a similar eruption in the same location one and a half years before. At that time the condition had disappeared spontaneously. About six months later the patient ceased working, and shortly after resuming his work the dermatitis reappeared. He stated that when he ground garlic into the meat, he noticed an immediate smarting of the involved area. I made patch tests on the left upper arm. Within five minutes he complained of intolerable burning at the site of the patch test. Removal of the patch disclosed an acute edematous area measuring ¾ by ½ inch (2 by 1 cm.) which was already vesicular. This reaction persisted and was still visible one month later. Ingestion of garlic caused no cutaneous reaction but produced severe cardiospasm immediately.

The location of the dermatitis is explained by the fact that the patient cleaned the debris from the guard of the meat grinder by passing his left forearm over it.

The dermatitis cleared in three weeks, when it was covered with a protective paste while the patient was at work.

408 Lincoln Street.

DERMATITIS FROM NYLON® HAIR NETS

C. RUSSELL ANDERSON, M.D.
BEVERLY HILLS, CALIF.

Recently, I have seen several women presenting an extremely severe acute dermatitis of the face, ears, neck and arms. Historically the dermatitis was of acute onset, and clinically it resembled an acute dermatitis seen in sensitivity to

hair dye. The history elicited the information that the dermatitis first appeared on the forehead and the ears. It was finally determined that these patients were allergic to brown nylon® hair nets which they purchased at different variety stores.

These nylon® hair nets were used for various purposes, such as keeping the hair in place after a wave set or keeping the hair from being mussed up while the patient was sleeping. Strongly positive reactions to patch tests were obtained. The patients were tested with items such as various dyes and nail lacquers, and no cross sensitivities were demonstrated. Patch tests were made on one woman with a nylon® hair net which had been washed several times, and a strongly positive reaction was obtained. None of these women were found to be allergic to nylon® stockings.

416 North Bedford Drive.

SIMPLE CLINICAL COLOR PHOTOGRAPHY

JOHN VAN DE ERVE Jr., M.D.
CHARLESTON, S. C.

Color photography is important in every dermatologic office. If one does not use color photography for teaching, it is often necessary and always convenient for one to have "before" and "after" photographs of lesions which are to be removed, and a recording of interesting and rare conditions. There may be medicolegal importance to such photographs, especially in regard to the treatment and removal of angiomas and carcinomas. There have been a number of excellent arrangements proposed and made available for clinical photography. Some have ground glass focusing; some have attached lights (but which require adjustment of controls for variation in the intensity of light with the variation in distance), and some use flash bulbs. Where cost of flash bulbs and films is a factor, the arrangement here shown will prove least expensive and, as I have judged from its use in my hands, very much simpler than the usual one.

The outfit described has been in use in my office for eleven years, with complete satisfaction. Two standard sizes were determined by extent of need. The 3 by 4 inch (8 by 10 cm.) field suffices to give close and intimate detail of practically all the usual dermatologic lesions. Photographs of this type account for about 85 per cent of the clinical photography in dermatology. The other 15 per cent is provided for by the 10 by 15 inch (25 by 38 cm.) field box frame outfit, which is sufficient to enable one to photograph the larger part of the distribution of lesions on an arm or leg or on the trunk. For photographs of lesions with generalized distribution, the camera is easily detached and used as any other camera, with adjusted lights and focusing.

Essentially, any good 35 mm. camera with an extension barrel may be used. The frame is made of brass strips, bolted and soldered together. The camera's focal distance with extension barrel in place (30 mm. barrel) may be easily determined with the use of a ground glass plate in the film area; the frame is then made of that length. The frame used for the 50 mm. lens (35 mm. negatives) shown in the illustration is 9¼ inches (24 cm.) long altogether and 5¼ inches (13 cm.) wide at the camera end, tapering to a square of 3 by 4 inches at the focused plane. With the strip to hold the flood bulb reflector the frame extends to a height of 5 inches at the camera end. When a 20 mm. extension barrel

is used to provide short focal distance, the distance from the lens to the focused plane is 143 mm. (5¾ inches). The small reflector with a no. 1 photoflood bulb is attached to the frame. The exposure may be calculated or adjusted by trial and error. Since the distance and light are always the same, once the proper settings for time and aperture are determined, they may be made and forgotten.

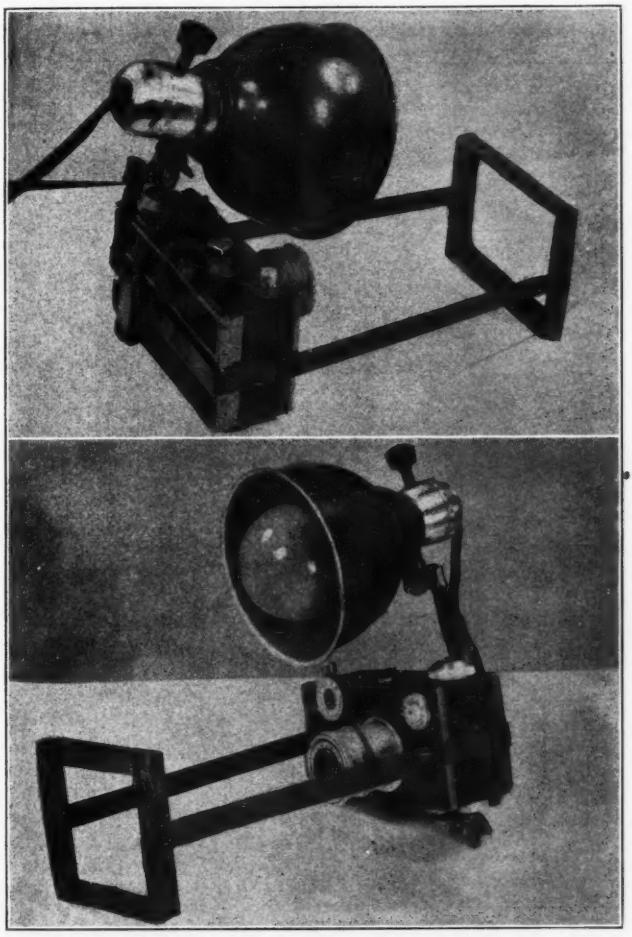


Fig. 1.—Apparatus providing 3 by 4 inch (8 by 10 cm.) field.

My camera has been used at a setting of f6.3 (actual aperture is about f.22) with a shutter time of 1/30 second for years. Once a year, the flood bulb should be replaced.

The camera outfit uses 35 mm. film only, and this least expensive form of color film may be used rather freely. No adjustments for light variation need be made;

no change in focusing or setting controls is necessary, and all that need be done is for one to pick up the outfit, turn on the flood bulb, set the square end frame, which is also the focused plane, against the skin or surface to be photographed and snap the shutter. This can all be done in a few seconds and need not interfere with the routine of a busy office.

The larger box frame is less convenient but often handy and useful. It might be more easily constructed of aluminum struts, which would make it much lighter.

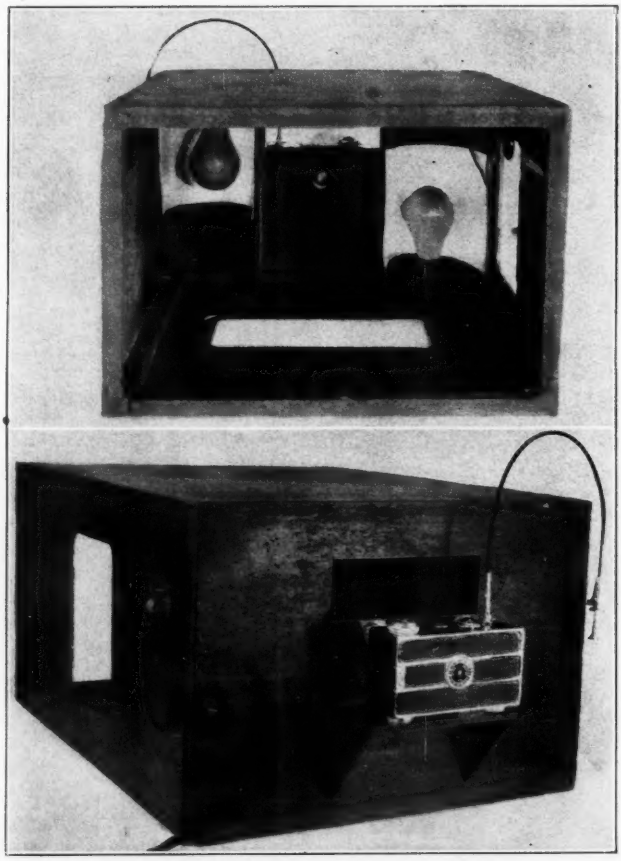


Fig. 2.—Apparatus providing 10 by 15 inch (25 by 38 cm.) field.

The area covered by the focused plane is approximately 10 by 15 inches. To obtain this field required, with the 50 mm. lens on the camera, a box 21½ inches (55 cm.) long, 16 inches (41 cm.) wide, and 11 inches (28 cm.) deep. The lens barrel is racked in and a —1 diopter auxiliary portrait lens is added. The camera is attached through its tripod socket to the frame of the box. It may readily be removed for regular focused distance photography.

Two by 2 inch (5 by 5 cm.) ready-mounted transparencies in full color taken with these outfits have all the sparkling brilliance, lighting and sharp focusing that can be desired, at a minimum of time, inconvenience and cost.

77 Rutledge Avenue (37).

COMPARISON OF FINGER NAILS IN NEGROES AND WHITE PERSONS

ROBERT H. HARRIS, M.D.
LONG BEACH, CALIF.

Finger nail changes in a Negro woman with thyrotoxicosis were shown at the April 1948 meeting of the Chicago Dermatological Society. A statement by a surgeon interested in surgery of the thyroid that these changes were more often seen in the Negro aroused interest in possible differences between finger nails of the Negro and those of the white person.

*Presence and Absence of Lunulas on Finger Nails of Negroes and of White Persons**

Negroes							White Persons						
Case No.	Classification of Subject	1	2	3	4	5	Case No.	Classification of Subject	1	2	3	4	5
1.....	J.	x	o	o	o	o	1.....	Ad.	x	x	x	x	x
2.....	J.	x	x	x	o	o	2.....	J.	x	o	o	o	o
3.....	Ad.	x	o	o	o	o	3.....	Ad.	x	x	x	x	o
4.....	Ad.	x	o	o	o	o	4.....	J.	x	x	x	x	x
5.....	Ad.	Lx	x	o	o	o	5.....	J.	x	x	x	x	x
		Rx	x	x	x	o							
6.....	Ad.	x	x	x	o	o	6.....	Ad.	x	x	x	x	o
7.....	Ad.	x	o	o	o	o	7.....	J.	x	x	x	x	x
8.....	Ad.	x	o	o	o	o	8.....	Ad.	x	x	x	x	o
9.....	Ad.	o	o	o	o	o	9.....	Ad.	x	o	o	o	o
10.....	Ad.	o	o	o	o	o	10.....	Ad.	x	o	o	o	o
11.....	Ad.	o	o	o	o	o	11.....	Ad.	x	x	x	o	o
12.....	Ad.	o	o	o	o	o	12.....	Ad.	o	o	o	o	o
13.....	Ad.	o	o	o	o	o	13.....	Ad.	x	x	x	x	o
14.....	Ad.	x	o	o	o	o	14.....	Ad.	x	o	o	o	o
15.....	Ad.	x	o	o	o	o	15.....	Ad.	o	o	o	o	o
16.....	Ad.	o	o	o	o	o	16.....	Al.	x	x	o	o	o
17.....	J.	x	o	o	o	o	17.....	Ad.	x	x	o	o	o
18.....	Al.	x	o	o	o	o	18.....	Ad.	x	x	o	o	o
19.....	Ad.	o	o	o	o	o	19.....	Ad.	x	x	x	x	x
20.....	Ad.	o	o	o	o	o	20.....	Ad.	x	x	x	o	o
21.....	Ad.	o	o	o	o	o	21.....	Ad.	x	x	x	x	x
22.....	Ad.	o	o	o	o	o	22.....	Ad.	x	x	x	o	o
23.....	Ad.	x	o	o	o	o	23.....	Ad.	x	x	o	o	o
24.....	Ad.	x	o	o	o	o	24.....	J.	x	o	o	o	o
25.....	Ad.	o	o	o	o	o	25.....	Ad.	x	x	x	o	o

* Presence of a lunula is indicated by an x, and absence, by an o. In classification of subjects J stands for juvenile (1 to 10 years); Al, for adolescent (10 to 20 years), and Ad, for adult (over 20 years).

Twenty-five definitely white persons and 25 persons with definitely negroid characteristics were examined. These were both male and female, and of all age groups. It was found that the finger nails of the Negro seem to have a tendency to be longer and proportionately narrower than the nails of the white person. The outstanding difference was the presence or absence of the lunula. Eleven Negroes showed no lunula in any of the finger nails. Only 2 white persons showed

no lunula; these were of Lithuanian and Swedish-Irish descent. Eleven Negroes showed lunulas only on the thumb, while 5 white patients showed lunulas only on the thumb. Of the 25 Negroes, none had lunulas on all the finger nails. Of the 25 white persons 6 had lunulas on all the finger nails.

Both hands were examined, and the findings were almost uniformly bilateral (table).

The average finger nails of the Negroes in this series showed a comparative absence of lunulas.

The lunula, according to Burrows' investigations,[1] shows as an opaque, proximal, semilunar area, not because of any peculiarity of the nail plate but as a result of the reflected light from the surface of the junction of the matrix and

Finger nails of a Negro, showing longitudinal lines of pigmentation and absence of lunulas.

the connective tissue portion of the nail, the matrix not being adherent to the connective tissue in this area as elsewhere under the nail.

It was concluded that, although the findings reported here were true for a group, they might not hold true for an individual. Whether these findings explain any differences in pathologic changes of the finger nail is not known.

The accompanying figure shows definite Negro finger nails, with longitudinal lines of pigmentation and absence of lunulas.

305 Times Building.

1. Burrows, M. T.: The Significance of the Lunula of the Nail, Johns Hopkins Hosp. Rep. **8**:357, 1919; abstracted, Arch. Dermat. & Syph. **1**:68 (Jan.) 1920.

RESTRICTIONS REGARDING USE OF DIATHERMY APPARATUS

ANTHONY C. CIPOLLARO, M.D.
NEW YORK

The Federal Communications Commission has found it necessary to restrict the use of medical diathermy apparatus. After July 1, 1952, it will be illegal for one to use any diathermy unit the frequencies of which are not within assigned bands. Every new diathermy apparatus approved by the Commission will bear a name plate showing the F. C. C. type approval number. Most units now in use for medical diathermy do not conform to the new regulations. They will have to be discarded, or the room in which they are used will have to be shielded.

The Commission found it necessary to impose strict restrictions on the manufacture and use of medical diathermy apparatus because such equipment was interfering seriously with radio communications, including television. During the war, this type of interference was a major problem. Since a diathermy unit is a radio transmitter, the energy used to heat body tissue is picked up by radio receivers and causes static-like interference and can even blot out an image on a television reeciver screen.

New apparatus are assigned definite and limited frequencies of operation. To keep them within these prescribed channels various means of control have been devised. The most effective and therefore the most widely used one is crystal control apparatus. Crystals are pretty stabile and do not get out of order easily. If the crystal is fractured, the replacement cost is small.

If one wishes to retain and use one's old diathermy apparatus, it will be necessary to screen the treatment room so that all radio waves are confined within the room. This aim can be accomplished by the lining of the floor, ceiling, walls, doors and windows with grounded copper screening. After this has been accomplished the treatment room is inspected and a special operator's license is issued by the Federal Communications Commission.

Dermatologists employ diathermy currents for surgical purposes. Electrosurgical equipment is operated by a foot switch, and the operation is intermittent. Even this equipment interferes with radio communication, but the interference is negligible, and the Commission did not consider it necessary to include electrosurgical apparatus under the ruling.

A dermatologist may therefore keep on using his electrosurgical apparatus the way he has always used it for the purpose of destroying cutaneous lesions. However, he should not use his apparatus for medical diathermy and should not run it continuously.

Dermatologists who are purchasing new equipment will do well to inquire whether or not new models of electrosurgical equipment are to be built with circuits which do not interfere with radio communications. It may be possible that efficient, inexpensive crystal-controlled or high C circuit and self-excited oscillator circuit surgical diathermy units may be the vogue by 1952. If so, it is well for one to buy such equipment rather than the present radio-interfering surgical diathermy apparatus.

At the present time electrosurgical equipment does not have to be approved and it is not necessary for dermatologists to make any changes whatsoever in their present equipment. If any new regulations are promulgated by the Federal Communications Commission pertaining to apparatus currently used by dermatologists, I shall report them in the ARCHIVES OF DERMATOLOGY AND SYPHILOGY.

40 East Sixty-First Street (21).

From the New York Polyclinic Medical School and Hospital.

PITYRIASIS ROSEA ACCOMPANIED WITH BELL'S PALSY

LOUIS G. JEKEL, M.D.
PHOENIX, ARIZ.

Mild, and even severe, constitutional reactions accompanying pityriasis rosea have been reported many times, but involvement of the nervous system is rarely recorded. Von Szabóky,[1] who did refer to nervous manifestations, merely generalized on the subject by mentioning sweating, trembling, pallor and redness, headache and exaggerated reflexes.

Therefore, a case of pityriasis rosea accompanied with a unilateral paralysis of a facial nerve (Bell's palsy) is considered worthy of a report.

C. F., a 15 year old white schoolgirl, first became ill with the common cold, accompanying which was an unusually severe headache. Three days later there appeared an eruption consisting of one large spot and several smaller spots on the right side of the trunk. The eruption was symptomless. A day later the patient noticed a peculiar feeling in the left side of the face, with inability to smile normally and inability to close the left eye. There was a disturbance of taste on the left side of the tongue, but no other sensory changes were detected. The patient had no fever.

The urine contained a very faint trace of albumin and was entirely normal in other respects. A complete blood count was normal. Serologic tests for syphilis had negative reactions, as did agglutination tests for typhoid. The basal metabolic rate was normal (0).

The patient's physician made a diagnosis of complete paralysis of the left facial nerve (Bell's palsy).

The eruption was typical of pityriasis rosea.

Three weeks later, at the final observation, the patient had recovered completely and uneventfully from both the eruption and the paralysis.

15 East Monroe Street.

1. von Szabóky, J.: Beiträge zur Aetiologie der Pityriasis rosea, Monatsh. f. prakt. Dermat. **42**:495, 1906.

DERMATITIS ACCENTUATED BY GAUZE

Report of a Case

LESTER HOLLANDER, M.D.
PITTSBURGH

Miss F. J., a 27 year old librarian, was receiving treatment on account of a typical atopic dermatitis of long duration. Her forehead, neck, shoulders, antecubital fossae, wrists and arms presented patches of dermatitis in various stages of development. She also suffered from seasonal hay fever. Two other members of her family presented similar difficulty at various times.

Since the response of the skin to topical applications is always an unknown quantity at best, and much more so in patients presenting an atopic dermatitis, it is my custom to try out a number of test ointments at various affected areas before I decide which one is to be relied on.

I carried out a similar procedure in this instance. The test ointments were covered with gauze and then secured with a loosely applied roller bandage.

Within a short time the patient complained of burning at all the test areas. The applications were of course removed at once, with the use of warm mineral oil. Except for the fact that the dermatitis seemed more acute, nothing of note was recorded.

To permit the subsidence of the dermatitis accentuated by the test ointments, the patient was instructed to return in three days, having applied nothing to her skin and having refrained from washing during the interval.

On her return three areas of dermatitis were selected and bandaged with several layers of sterile gauze so that on each area there was the product of a different manufacturer. Within ten minutes burning was experienced at all the areas, and on the removal of the gauze dressings the observation of a noticeable increase in redness testified to the veracity of the patient's complaint.

Similar gauze patch tests were now applied to normal-appearing cutaneous surfaces and left in place for forty-eight hours. No reaction was noted at the end of this period at these sites.

I believe that accentuation of dermatitis as a result of sensitivity to gauze may occur more often than is generally suspected, as no one had called my attention to it.

631 Jenkins Building (22).

COMPOUND BENZOIN TINCTURE IN TREATMENT OF VESICULOBULLOUS LESIONS OF MUCOUS MEMBRANES

HENRY HARRIS PERLMAN, M.D.
PHILADELPHIA

It often happens that the dermatologist is concerned with vesiculobullous lesions of the mucous membrane of the oral cavity that tax all his skill as a therapeutist. Treatment with compound benzoin tincture has given excellent results in these cases, and, as there are no references to it in recent dermatologic literature, I wish to bring it to the attention of dermatologists.

Benzoin is one of the ancient drugs of pharmacy and has enjoyed its popularity under a masquerade of many romantic names, among them Turlington's balsam, friars' balsam, Wade's balsam, balsam de malthe, Jesuit's drops, St. Victor's balsam, Persian balsam, Swedish balsam and Jerusalem balsam. It is official in the United States Pharmacoepeia and the British Pharmacopeia under the title tinctura benzoini composita. It is prepared by the maceration of a mixture of benzoin, aloe in the form of a moderately coarse powder, storax and tolu balsam in strong alcohol for three days. Then the mixture is filtered and enough alcohol added so that the tincture contains 74 to 80 per cent by volume of alcohol. Because of this strong alcoholic content the preparation is irritating to broken tissues. Downing and Stoklosa [1] developed a nonirritating ointment in which the compound tincture evaporated to the consistency of an extract is incorporated in a zinc oxide base.

The antiseptic effect of the tincture is probably dependent on the benzoic and cinnamic acids contained in the benzoin and storax, two of the active ingredients of the compound, while the strong alcoholic content of the pharmaceutic preparation

1. Downing, J. G., and Stoklosa, M. J.: Compound Tincture of Benzoin in Ointments, Arch. Dermat. & Syph. **54**:714 (Dec.) 1946.

possibly has some additional antiseptic and dehydrating effect on the edematous tissue.

In the following report, the application of compound tincture of benzoin to the oral lesions resulted in the elimination of pain and the improvement of the lesions after the failure of many other indicated methods.

REPORT OF A CASE

L. C., 19 years of age, a college student, suffering from recurrent episodes of blisters in her mouth, was referred to me in October 1947. In November 1945 gingival lesions involving her throat and buccal areas developed. The temperature rose at night (101 to 103 F.) but receded in the morning. The gingival lesions, which principally were gray vesicles, healed without scarring. But they spread over the buccal surfaces, tongue and fauces. There was submaxillary adenitis. Treatment consisted of the use of salicylates and sulfonamide drugs and the intramuscular injection of 300,000 units of penicillin. The temperature became normal in a week, and the patient was well in two weeks. All laboratory tests (including the smear for Vincent's angina) had negative results. Alkaline mouth washes and dyes had been used without effect.

Two months later there was another attack, which commenced with a small ulcer, resembling aphthous stomatitis, under the upper lip. It spread rapidly, involving the whole mouth, with vesicles and small bullae that changed into crusts, especially on the vermilion border of the lip. There was edema of the lips and mouth, conjunctivitis and photophobia. The condition responded well to large intravenous injections of preparations containing the vitamin B complex. The patient was ambulatory and became well in six weeks.

On about May 25, 1946, the patient acquired an ulcer under the upper lip which spread rapidly until the tongue, cheeks, vermilion border and most of the oral mucosa were involved. There was conjunctivitis, and the edema of the pharynx and the oral mucosa was so severe that eating and swallowing became very difficult. The condition did not respond to treatment with 300,000 units of penicillin and 15 grains (1 Gm.) of methenamine, the latter administered three times daily. The patient had to be hospitalized. The temperature, blood picture and blood chemistry were normal. The Wassermann reaction of the blood was negative. Treatment consisted of intravenous injections of methenamine, 15 grains each, for three days, and two whole blood transfusions. The patient was discharged in nine days in good condition.

In April 1947 the patient experienced another attack similar to the preceding one. Five doses of 15 grains of methenamine were given intravenously over a ten day period. Simultaneously vaccinations with smallpox virus were performed without their achieving a "take." The episode was aborted, and the patient remained ambulatory.

On Oct. 17, 1947, vesicular lesions developed on the mucous membranes of the upper and lower lips. They spread until the entire oral mucosa was involved. The conjunctivas and the skin remained free of lesions. The vesicles ruptured and formed crusts. The patient remained afebrile but was unable to take food by mouth because of great pain. Even the sipping of milk through a tube was very painful. There was no "take" to vaccination with smallpox virus. Intravenous injections of methenamine were given as before. The mouth was given a cleansing with a potassium permanganate solution (1:2,000) followed by a wiping of the lesions with liquid petrolatum. No relief was obtained. Then full strength compound benzoin tincture was applied with a cotton applicator. There was almost immediate relief from pain, and within a few hours there was a noticeable decrease

in edema of the lips. The patient was able to take food, and in a few days the lesions in the mouth subsided. During those few days the patient kept applying the compound benzoin tincture herself every few hours. There has been no recurrence since that time.

I have used compound benzoin tincture with excellent results in treatment of herpes simplex of the lips, aphthous stomatitis and lesions of so-called "trench mouth" in infants and Vincent's infection. Although I have had no experience with its use in treatment of oral lesions of pemphigus and epidermolysis bullosa I think it would be of help. It has given relief of pain in a case of lingua geographica in a 6 year old white boy.

SUMMARY AND CONCLUSIONS

A case of erythema multiforme exudativum, characterized by recurrent episodes of vesiculobullous lesions on the lips and oral mucosa, is reported. Topical therapy consisting of the use of various alkaline mouth washes and dyes and local applications of silver nitrate failed to improve the lesions of the lips and the oral mucosa.

The aforementioned vesiculobullous lesions promptly responded to topical applications of compound benzoin tincture U. S. P.

Some of the commoner dermatologic entities affecting the mucous membranes of the lips and mouth in which the topical application of the official compound benzoin tincture has proved of value are listed.

1726 Pine Street.

LICHEN PLANUS HYPERTROPHICUS

Possiible Clue to Etiology

CHARLES C. DENNIE, M.D.
AND
FRANCIS P. COOMBS, M.D.
KANSAS CITY, MO.

A. H., a 58 year old married woman, was first seen by us on Nov. 4, 1947, and a diagnosis of lichen planus hypertrophicus of the anterolateral surface of the left thigh was made. Pronounced varicose veins of both legs were found. The lesions had first appeared one year previous to the patient's first visit. Leading from the area was a moderately large varicose vein, tortuously running toward the saphenous vein at the junction of the upper and the middle third of the thigh. This varix had been present for some time previous to the appearance of the lesions. Biopsy showed typical lichen planus hypertrophicus.

Microscopic observations were as follows: The keratin layer was thickened. One follicle was widened, with decided keratotic plugging. Relative and absolute hyperkeratosis, an increase in the stratum granulosum, acanthosis, slight liquefactive degeneration of the basal cell layer and mild lymphocytic infiltration in the upper portion of the cutis, with some histiocytosis around the keratinized follicle, were seen.

The patient related that in 1940 she had had a patch of identical lesions on the anterior surface of the lower part of the left leg, also associated with a varicose

vein. The lesions remained despite local applications, but, almost immediately after the patient's physician injected the varicose vein, the lesions flattened and disappeared, leaving no scars.

The current patch of lichen planus hypertrophicus was treated with camphor, and solution of coal tar N. F. in calamine lotion locally, and bismuth subsalicylate and liver injection U. S. P. given intramuscularly each week for a total of five doses. On December 28, the patient complained of tenderness and redness of the vein leading from the present area of lichen planus hypertrophicus. The vein was very tender on pressure and suggestively cordlike. Within one to two weeks, the lesions were flat and many had completely disappeared. Subsequent to this period, all varicose veins involved in this leg were ligated and removed, and all lesions disappeared.

Many etiologic possibilities have been suggested, including nervous shock, foci of infection, toxemia, neurovascular instability and a virus. It seems logical to assume that in this case the poor circulation was the principal factor in the development of the lichen planus hypertrophicus, since twice in the same person the lesions cleared when better circulation was established.

This case is reported, not to suggest that all cases of the disease are associated with a local vascular disorder, but to aid in finally discovering the etiologic factors which are important in the formation of lichen planus hypertrophicus.

1524 Professional Building (6).

RINGWORM OF THE SCALP OF AN ADULT

Report of a Case

VICTOR R. HIRSCHMANN, M.D.
and
SIDNEY OLANSKY, M.D.
DURHAM, N. C.

Ringworm of the scalp is a common disease among children in the United States. The literature is replete with reports of numerous epidemics of the type due to Microsporum audouini as well as endemic cases resulting from infection with the types of fungi occurring on animal hosts. Ringworm of the scalp of adults, however, is unusual and warrants attention, if for no other purpose than to renew awareness of its existence and the need for considering it in the differential diagnosis of diseases of the scalp in persons beyond puberty.

Fox and Fowlkes[1] reviewed the subject of ringworm of the scalp in adults in 1925. Since that time there has been no comprehensive consideration of its morbidity in the literature. Isolated reports of cases are found. In the review by Fox and Fowlkes it was found that 53 cases, including their own, had been reported. Of these 53 cases only 4 were caused by M. audouini, the remainder being due to trichophytons, Microsporum lanosum and unidentified fungi.

From the Division of Dermatology and Syphilology of the Department of Medicine, Duke University School of Medicine.

1. Fox, H., and Fowlkes, R. W.: Ringworm of the Scalp in Adults, Arch. Dermat. & Syph. **11**:446 (April) 1925.

Rothman and associates [2] explained the relative immunity of adults to ringworm of the scalp on the basis that hair fat of the adult is five times as fungistatic as is that of children. The fatty acids of the adult scalp are almost invariably of a high enough concentration to inhibit the growth of M. audouini. Apparently, however, they are not adequate to inhibit the growth of Achorion schoenleini, Trichophyton gypseum or M. lanosum, to which adults are susceptible to a varying degree.

REPORT OF A CASE

J. G. J., a Negro man aged 40, was seen first in the Duke Hospital dermatology clinic on Dec. 23, 1947, because of "scalp trouble."

Examination revealed that there were two quarter dollar–sized areas of alopecia in the right temporal region and the posterior part of the left temporal region. These lesions were sharply demarcated with a slightly raised border. The hair was sparse in the lesions and broken off. The patient at this time stated that these areas had been present for a few months and had been gradually becoming larger. Subjective symptoms were exclusively those of itching. The reactions to the Wassermann, Kahn, Kline and Mazzini tests were reported as negative on December 17.

Because of the active border and the fractured hairs in the center of the lesion, the distinct probability of tinea capitis was considered. Hairs were removed for direct examination and culture. Potassium hydroxide preparation of hairs revealed numerous spores of the ectothrix variety. The hair was also noted to fluoresce under the Wood light. An attempt to obtain a history of exposure revealed that the patient had been exposed to dogs and cattle during the past few months but to the best of his knowledge not to any persons with ringworm of the scalp. He was the only member of his family with the complaint. Photographs taken at the time reveal the extent of the disease (fig.). Expectant therapy was instituted pending a report on the culture, and a preparation of 5 per cent precipitated sulfur in half-strength benzoic and salicylic acid ointment N. F. was prescribed for local use after a daily shampoo of the scalp.

Other findings, both physical and laboratory, were not pertinent and are not incorporated in this report.

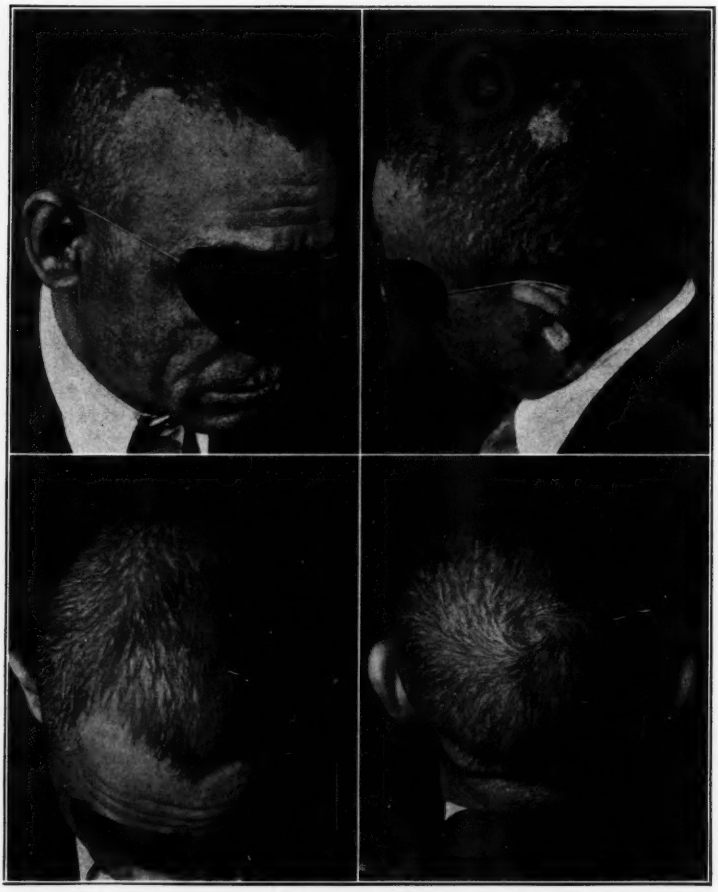
On December 30 Dr. Norman F. Conant reported that the responsible fungus was Microsporum audouini. It was decided to epilate the scalp. On Jan. 13, 1948, an epilating dose of roentgen radiation was given by the Adamson-Kienböck procedure with a total dose of 360 per port using factors of 90 kilovolts and 5 milliamperes at a 10 inch (25 cm.) distance without additional filtration. On the next visit, on February 12, epilation was complete except on one small area in the left temporal region. Examination under Wood's light at this time revealed a few fluorescent hairs. The remaining hairs were manually epilated. The patient was placed on the following treatment regimen: (1) daily scrubbing of the scalp with soap, followed by an application of a solution of sodium propionate; (2) application of copper undecylenate ointment to the scalp each night; (3) wearing of a cotton cap, which was changed daily and washed.

He was seen again on February 26, at which time no fluorescent hairs could be demonstrated. The routine of therapy was unchanged. On April 1 three fluorescent hairs were found on the scalp and there was a mild generalized edema of the

2. Rothman, S.; Smiljanic, A. M., and Weitkamp, A. W.: Mechanism of Spontaneous Cure in Puberty of Ringworm of the Scalp, Science **104**:201 (Aug. 30) 1946.

skin of the entire scalp. The hairs were manually epilated and 5 per cent salicylanilide ointment substituted for the copper undecylenate ointment in the therapeutic regimen.

On May 6 the scalp was found to be free of fluorescence and there was a good regrowth of hair. At this time the patient was considered cured (fig.).



The upper photographs show the patient before the beginning of treatment, with areas of alopecia in the right temporal region and the posterior part of the left temporal region. The lower photographs, of the patient after treatment, show a good regrowth of hair.

COMMENT

A case of ringworm of the scalp due to M. audouini in an adult is reported. A satisfactory clinical response was obtained by means of roentgen epilation and topical applications of conventional therapeutic agents.

Society Transactions

BRONX DERMATOLOGICAL SOCIETY

Charles Wolf, M.D., *President*

Henry Silver, M.D., *Secretary*

Jan. 15, 1948

Granuloma Inguinale Treated with Streptomycin. Presented by DR. THEODORE ROSENTHAL.

A. J., a Negro aged 39, was admitted to the Central Social Hygiene Clinic of the New York Department of Health on Dec. 5, 1947.

An indurated ulcer, 1 cm. in diameter, was situated on the corona of the penis. Donovan bodies were demonstrated in the lesion, which had been present for the past six weeks.

The patient was given streptomycin suspended in peanut oil and white wax U. S. P., each cubic centimeter containing 300,000 units. He received a total of 20 Gm. in a course of single daily intramuscular injections for twelve days, except Sundays. The lesion was completely healed on December 18, the date of the last injection, and has remained healed.

Repeated dark field examinations were negative for Treponema pallidum. The Wassermann reactions of the blood were negative on December 2 and 18 and on Jan. 15, 1948. Reactions to the Frei test were negative.

Granuloma Inguinale Treated with Streptomycin. Presented by DR. THEODORE ROSENTHAL.

P. F., a Negro aged 41, had a typical granulomatous ulcer on the penis. The condition had been present for the past three years. Donovan bodies were found on admission, on Feb. 19, 1947.

The patient received injections of stibanose® (the diethylaminoethanol salt of sodium antimony gluconate), and the lesion at first healed but later became worse. On December 16 there was a 1 cm. cuff around the corona of the penis, consisting of beefy red granulations. From December 17 to December 31, the patient received seven intramuscular injections of streptomycin, a total dose of 10,800,000 units. He took the treatment irregularly. He has shown considerable improvement, although the lesion has not healed completely.

The Wassermann reaction of the blood was negative. Reactions to the Frei test were negative.

Granuloma Inguinale Treated with Streptomycin. Presented by DR. THEODORE ROSENTHAL.

J. G., a Negro aged 21, had a lesion which had been present for four weeks.

On the prepuce there was a granulating ulcer, 2 cm. in diameter. Donovan bodies were found in the lesion. The Wassermann reaction of the blood was negative.

During the period from Dec. 19, 1947 to Jan. 9, 1948, except on Sundays, the patient received fourteen daily intramuscular injections of an aqueous solution of streptomycin, 0.25 mg. per cubic centimeter. The total amount given was 20 Gm. The lesion has healed completely, with depigmentation remaining.

Granuloma Inguinale Treated with Streptomycin. Presented by DR. NATHAN SOBEL.

H. S., a Negro aged 24, on Nov. 3, 1947 had a lesion which had been present for the past three weeks.

On the frenum, glans penis and inner surface of the prepuce there was an irregular, granulating ulcer in which Donovan bodies were demonstrated.

The patient received daily injections of streptomycin, except on Sundays, for a total of 20 Gm. The lesion healed. On Jan. 14, 1948, there was an elevation in a part of the previously affected area and Donovan bodies were again found.

The Wassermann reactions of the blood were negative on Oct. 22, 1947 and on Jan. 8, 1948.

Granuloma Inguinale Treated with Streptomycin. Presented by DR. JULIUS H. POLLOCK.

J. J., a Negro aged 46, had a lesion of ten years' duration.

The lesion was granulomatous and surrounded the entire corona of the penis. The glans penis showed depigmentation, and the shaft was swollen and distorted. Donovan bodies could not be demonstrated, but the diagnosis of granuloma inguinale was considered justifiable.

The patient was treated with antimony preparations, with little benefit. On July 15, 1947, he was admitted to the New York City Hospital, where he was given stibophen (fuadin®), 5 cc. daily for two weeks. At irregular intervals he received seven additional injections of stibophen. On Jan. 9, 1948, he returned to the clinic. On reexamination the lesion was found aggravated and painful. Treatment with streptomycin was instituted. After the first injection of an aqueous solution of 1.5 Gm. of streptomycin the pain stopped and the local inflammation subsided.

The patient has received a total of 9 Gm. of streptomycin to date in daily intramuscular injections of 1.5 Gm. The lesion shows continued improvement.

DISCUSSION ON PRECEDING CASES

DR. THEODORE ROSENTHAL: The treatment of granuloma inguinale with streptomycin has already been reported on. However, we have employed an ambulatory method. The original information on the use of streptomycin was of such nature as to make one believe that the drug should be used with great caution and that frequent serious reactions were to be expected. However, no evidence of pronounced toxicity was encountered in this small series. The drug was administered either in aqueous solution or in white wax U. S. P. and peanut oil. The streptomycin for the latter form was mixed in our own laboratory. Apparently there was no great difference in therapeutic effectiveness between streptomycin in aqueous solution and that in peanut oil and white wax.

Among the 5 patients treated, one relapse has already occurred. Other workers have reported that relapses are to be expected. One patient, who has been under observation for the longest period, approximately three months, is completely well. Except for some painful local reaction in the buttocks following injection, there were no untoward reactions. Injections were given once daily in the average dose of 1.5 Gm., for a total of 20 Gm.

DR. NATHAN SOBEL: This treatment has been reported as effective. When smears are taken in follow-up examinations there is said to occur actual fragmentation, followed by disappearance of the organism in six days, on an average, and sometimes as early as in two days. We have observed but one relapse among the

patients who were adequately treated. It is true that administration of antimony compounds during the early stage of the lesions results in decided clinical improvement. However, even after several months of this therapy Donovan bodies can still be demonstrated in the lesions.

Another interesting feature noted in this series, characteristic of most cases of granuloma inguinale we have seen recently, is that small lesions which simulate the primary lesions of syphilis are encountered. Furthermore, it is unusual in clinical practice for one to see extensive chronic lesions that occur in the genitocrural areas. Ambulatory treatment with streptomycin is well tolerated. It has been reported that injection of aqueous streptomycin is extremely painful and cannot be done without hospitalization of the patient. My associates and I, on the other hand, encountered little difficulty. I have not added any procaine hydrochloride (novocain), as has been done elsewhere. If the ambulatory method of administering streptomycin should prove practicable, it could be extended to other diseases, such as tuberculosis of the skin.

DR. ARTHUR SAYER: I think the presenters are to be commended for the successful treatment of these difficult cases. However, I wish to call attention to the fact that the doses employed are rather small, as compared with those used by Greenblatt and his co-workers. In their series the daily dose of streptomycin was as high as 4 Gm. It is probable that in early cases a smaller dose of streptomycin may be effective. However, in cases of longer duration, I am certain that larger doses will be required.

I have recently had the opportunity of observing a patient with granuloma inguinale of two years' duration at the United States Naval Hospital in St. Albans, N. Y., who was treated with streptomycin. He was given 0.6 Gm. intramuscularly every three hours for five days, for a total of 20 Gm. A satisfactory result was obtained; the lesion healed completely.

I believe that streptomycin is by far the best means of treating granuloma inguinale and that the most satisfactory dosage will be determined by future experience.

DR. CHARLES R. REIN: It is of interest that none of the patients presented had any evidence of pediculosis pubis. In a large series of patients with granuloma inguinale observed in Washington, D. C., Dr. Donald Butts was able to demonstrate Phthirus pubis in the majority of persons. He also found the Donovan bodies in the lice themselves and believed that the parasites played an important role in the transmission of the disease.

DR. WILLIAM LEIDER: One of the most interesting questions about this disease has not been raised tonight, except for the observations mentioned by Dr. Rein. I refer to the question of the mode of transmission of the disease. Are we justified in labeling the disease as venereal simply because the lesions occur in the anogenital region? It is well known that the disease is rarely found in contacts or in marital partners of patients with active lesions. Is it possible that, as in lymphogranuloma venereum, there exist carriers of the organisms who have no manifest lesions?

DR. THEODORE ROSENTHAL: It is not possible, in attempting treatment with a new drug, for one to hit on the ideal dosage immediately. Although Dr. Sayer reported the experience of the Atlanta group, who used a variety of doses, he himself used the dosage of 20 Gm. which we have used empirically, administered at the rate of 1.5 Gm. daily. If the dose proves too small we can increase it. As to Dr. Leider's comment, it is true, of course, that the incidence of conjugal infection is exceedingly small; a great deal of information still remains to be

elicited on the communicability of granuloma inguinale. I myself have never seen patients with granuloma inguinale who had pediculosis pubis. I have always believed the secretion of the skin of the Negro to be unfriendly to lice.

DR. NATHAN SOBEL: I should like to mention the experience of the Atlanta group (Kupperman, H. S.; Greenblatt, R. B., and Dienst, R. B.: Streptomycin in the Therapy of Granuloma Inguinale, *J. A. M. A.* **136**:84 [Jan. 10] 1948). They noted a number of relapses with amounts of less than 2 Gm. daily, with a total of eight relapses in 91 cases. They retreated 7 patients of that group with a 4 Gm. daily schedule and obtained good results. One of their patients, whose case was resistant to streptomycin, was treated with antimony preparations and finally was cured.

Another point not touched on is the controversial nature of the causative organism. K. Anderson, who originally cultured it, believed it to be a bacillus and named it Donovania granulomatis.

On the question of transmission, I wish to cite a case observed at the clinic of the Health Department which my associates and I believe is the only case of a known sex contact who contracted this disease. We have never seen P. pubis in our group of cases.

Granuloma Inguinale with Pseudobubo, Adenitis and Bubonulus. Presented by DR. NATHAN SOBEL.

R. C., a Negro aged 27, on Jan. 14, 1948 had a lesion which had been present for six weeks.

There is a beefy, granulomatous lesion about 2.5 cm. in diameter involving the area of the frenum. In the right inguinal region there is a pseudobubo with a granulomatous ulceration. An elevated lesion the size of a dime and corresponding to the dorsal lymphatic vessel is present on the dorsum of the penis near the base. In the left groin there is an enlarged gland, and the overlying skin shows no evidence of erythema.

Donovan bodies were found in the lesions of the glans penis and also in the material aspirated from the intact enlarged inguinal node.

DISCUSSION

DR. JULIUS H. POLLOCK: I wish to stress the striking feature which Dr. Sobel's case exemplifies, namely, the lymphatic spread of the disease in a patient with a primary lesion of granuloma inguinale on the glans penis. A bubonulus appeared, followed by breaking down of the inguinal nodes and the overlying skin. This picture certainly upsets our previous conception of this disease that the method of extension is purely cutaneous; this patient's case shows that the true nature of the spread is via the lymphatics, with secondary cutaneous involvement at distant sites from the primary inoculation on the penis.

DR. NATHAN SOBEL: Greenblatt expressed the opinion that the lesions in the genitocrural areas may start with a small lesion on the penis, which heals and is followed by involvement in the groin. In other words, the spread is by the lymphatics as well as by direct autoinoculation. It has been known for some time now that the lymphatics may be involved. This is the second case of bubonulus occurring in granuloma inguinale that I have seen. Dr. Pensky and I previously reported a similar case (ARCH. DERMAT. & SYPH. **48**:494 [Nov.] 1943).

Localized Amyloidosis Cutis. Presented by DR. JULIUS H. POLLOCK.

A Case for Diagnosis (Dermatitis Herpetiformis? Generalized Neurodermatitis?). Presented by DR. ALEXANDER A. FISHER.

Tuberculosis Colliquativa Treated with Promin® Jelly. Presented by DR. JOHN GARB.

K. B., a Negro woman aged 37, was presented before the New York Dermatological Society on April 24, 1945, by Dr. F. Wise with the diagnosis of tuberculosis of the skin (ARCH. DERMAT. & SYPH. **55**:587 [April] 1947.) The case is presented again to detail the additional investigations and to show the therapeutic effect of promin® (sodium p, p'diaminodiphenylsulfone-N,N'didextrose sulfonate) jelly.

DISCUSSION

DR. ALEXANDER A. FISHER: Since tuberculosis is a deep process, how can one explain the action of superficially applied promin® jelly?

DR. FRANK E. CROSS: The patient seems to have shown complete healing one week after the treatment with promin® jelly. However, the patient was previously treated with roentgen rays which, as known, have a cumulative effect. It is, therefore, difficult to decide which agent benefited the patient. It would have been better had some lesions been treated with roentgen rays and others with promin® jelly in order for the efficacy of the two to be determined.

DR. JOHN GARB: In answer to Dr. Fisher, the tuberculous ulcerations were freely exposed, and the promin® jelly came into direct contact with them. The promin® jelly was applied a week after the last roentgen treatment was given. Eight days later the patient stated that she had no more pain. In five weeks most of the lesions were closed, and in seven weeks they were completely healed; they have remained so since. Delayed action of roentgen rays can, therefore, be ruled out, since no noticeable improvement was observed during the six months of roentgen therapy. Rapid healing took place only after promin® jelly was applied to the lesion.

Morphea, with Pigmentation and Atrophy. Presented by DR. NATHAN SOBEL.

S. F., a woman aged 31, was first seen by me on Dec. 10, 1947, at the Skin and Cancer Unit of the New York Post-Graduate Hospital and Medical School. The condition she presented had persisted for the past ten years.

Over the right hypochondrium, extending to the midflank. there is a horizontal plaque with pigmentation and thickening in some areas. A similar plaque extends from the right breast to the lower part of the scapula. At the level of the umbilicus there are two areas showing pigmentation and definite atrophy of the skin. On the inner aspect of the right arm there is an irregularly outlined, whitish, elevated lesion the size of a quarter, with a hyperpigmented border. This lesion has been present for the past four months.

The Wassermann reaction of the blood was negative. The basal metabolic rate was —2 per cent.

DISCUSSION

DR. MAURICE UMANSKY: I was not convinced that the patch on the abdomen showed atrophic skin. Only microscopic evidence of destruction of the elastic tissue would be proof of atrophy. Pigmentation, on the other hand, is a frequent sequela of an old healed patch of localized scleroderma. The patch on the elbow is evidently of recent date; in contrast to the older lesions, it has no pigmentation.

DR. HENRY SILVER: This is the second instructive case of localized scleroderma and atrophy presented before this society. In Dr. Rein's case circumscribed patches of morphea and atrophy were present in the same patient. In the discussion I pointed out that his case may be used as an example by those who believe that atrophy and scleroderma are one entity. The case shown at this time is not clearcut. The patches of morphea can, of course, be readily diagnosed. There is some atrophy around the sclerodermatous areas. When dealing with these circumscribed, parchment-like lesions, it is difficult at an early stage for one to differentiate between localized scleroderma and localized atrophy. As the patch progresses into atrophy it shows the typical wrinkling and softness, and the palpating finger feels the loss of elastic tissue. In contrast, the plaque of scleroderma shows the hardness, the glistening, the whiteness and the other features well demonstrated in Dr. Sobel's case.

DR. NATHAN SOBEL: About one year ago the patient was apparently treated with extract of the pancreas, without benefit.

Necrobiosis Lipoidica. Presented by DR. CHARLES R. REIN and DR. NORMAN B. KANOF, Washington, D. C.

DISCUSSION

DR. HERMAN BEERMAN, Philadelphia: Can Dr. Sachs explain the presence of giant cells in the histologic picture of necrobiosis lipoidica?

DR. WILBERT SACHS: In necrobiosis lipoidica with or without diabetes it is common for one to find a large number of giant cells, whereas in granuloma annulare these cells may not be present.

DR. CHARLES LERNER: Is there any history of repeated trauma in the corresponding areas of the tibias?

DR. MORRIS LEIDER: Last year I presented before this society a case that was the exact likeness of this one, except that it was of a male Naval officer and more extensive. I wish to raise at this time the question of nomenclature and its propriety in this dermatosis. Urbach named the condition necrobiosis lipoidica diabeticorum. Since then the engaging factor of diabetes and hypercholesteremia seems to have lost importance. Recently, pathologists' discussions have suggested that histologic evidence of fat in the lesions is not indispensable to the microscopic picture. Thus, the word "necrobiosis" alone, which in itself is a bit irrational, is left. There are plenty of suggestions in both the clinical and histologic pictures of relation to an admitted tuberculoderma-like erythema induratum and a possible tuberculoderma-like granuloma annulare. Moreover, similarity to morphea and localized scleroderma is found in some cases (Goldsmith, W. N.: Recent Advances in Dermatology, Philadelphia, P. Blakiston's Son & Co., 1936). The prejudice of metabolic disturbance in Urbach's widely accepted title is a bit too persistent and tends, I think, to prevent examination of other possibilities of causation.

DR. WILBERT SACHS: The pathologist cannot say whether a patient has diabetes or not, from examination of a section of the skin. There is some necrosis present, and I believe that the term necrobiosis lipoidica is a good one for this condition; it is the responsibility of the clinician, and not of the pathologist, to add whether the patient has diabetes or not.

DR. MAX JESSNER: The case of the Naval officer mentioned by Dr. Leider presented the identical clinical picture, but there was no fatty degeneration. What one calls necrobiosis is a gradual degeneration leading to necrosis, and in typical cases there is usually a deposit of fatty substance.

DR. PERRY SACHS: The reported cases show a fatty deposit in the connective tissue. However, recently, stains for fat on frozen sections were done in a few cases of necrobiosis, and no increase of fat was found.

DR. HENRY SILVER: I know that Dr. Leider is interested in dermatologic terminology, if I may judge from his recent article (A Philological Note on a Certain Classical Suffix Commonly Used in Dermatologic and General Medical Nomenclature, *J. Invest. Dermat.* **9**:213 [Oct.] 1947). Oppenheim, who observed the first case of necrobiosis, thought of a peculiar type of atrophy and named it dermatitis atrophicans lipoides diabetica. It was Urbach who studied subsequent cases thoroughly and introduced the term of necrobiosis lipoidica diabeticorum. When reports of cases in persons who did not have diabetes began to accumulate, the question arose, shall we continue with the old term or drop the "diabeticorum"? The International Committee on Nomenclature decided to retain the name of necrobiosis lipoidica diabeticorum. The reason given was that in some of the cases without diabetes diabetes may later develop or be shown in the family history.

DR. CHARLES R. REIN: There was nothing in the history to denote any change in the patient's dietary regimen immediately prior to the onset of the eruption. I agree with Dr. Lerner that trauma plays an important role in this disease. In this patient there developed new circumscribed lesions of necrobiosis in areas of dermatitis caused by adhesive plaster. It would be of interest to note whether similar lesions of necrobiosis could be produced in experimentally traumatized areas.

Infantile Eczema in Twins. Presented by DR. DAVID BALLIN.

Lichen Planus et Hypertrophicus. Presented by DR. FRANK E. CROSS.

Charles Wolf, M.D., *President*
Henry Silver, M.D., *Secretary*
Feb. 19, 1948

Xanthine Pigmentation of the Palms and Soles. Presented by DR. CHARLES WOLF.

R. F. M., a woman aged 43, born in Russia, had had an enucleation of the left eye after an injury and had had a hemorrhoidectomy. The family history reveals that a sister also has a yellowish pigmentation of the palms.

The patient has been an avid eater of leafy, green vegetables and carrots since childhood and prefers vegetables to any other type of food. She also consumes a fair amount of fruit. She developed an appetite for vegetables in her early years of life, which she spent on a farm.

The palms show thickened plaques with a canary yellow discoloration, this pigmentation extending to the fingers and nails. The soles are similarly affected. There is a faint yellowish discoloration on both sides of the neck and over the shoulders in the area subject to friction from the underwear straps.

DISCUSSION

DR. WILBERT SACHS: Can the presenter state whether the patient has carotenemia or a yellow discoloration from some other source?

DR. FREDERICK REISS: This case is typical of what is also called carotenosis of the skin (aurantiasis cutis [Baeltz]), and the peculiar feature of the case is the limitation to the palm and soles. The discoloration was first noticed on the palms

in most of the patients observed by me. I saw a similar condition in a Chinese girl who ate twenty oranges daily. The patient presented indulged in similar eating habits, consuming quantities of carrots.

DR. ERNEST W. NATHAN: It is difficult to make a definite diagnosis in this case because the patient presents hyperkeratosis of the palms, which is often accompanied by a yellowish tint. I am not quite sure that this is a case of carotenosis but would favor hyperkeratosis with yellowish discoloration, as is commonly seen in housewives. The soles are by far more characteristic than the palms. It should be pointed out that other parts of the body did not show any yellowish discoloration.

DR. DAVID B. BALLIN: In a case of doubtful diagnosis it should not be difficult to prove carotenemia. When the blood is allowed to settle, the serum will show the striking golden orange color. The grade of discoloration may vary and is at times pronounced. I saw recently a case of a light-colored Negro who showed a pronounced golden color.

DR. CHARLES WOLF: The discoloration on the sides of the fingers, on the sides of the neck and over the shoulder strap region speaks in favor of hematogenous origin. I doubt that the patient consumes enough carrots to produce carotenemia. I do not think that diet is the causative factor in the case. The patient is a vegetarian but does not like leguminous vegetables and favors the leafy ones. These contain xanthine, which is a derivative of purine. On purine metabolism in the liver xanthine and uric acid are formed. Further studies will determine whether there is an excess excretion of uric acid in the urine or increased uric acid in the blood. I do not regard the case as one of carotenemia, but rather as one of hyperxanthinemia.

Xanthomatosis, with Lesions on Elbows, Knees and Eyelids. Presented by DR. MAURICE UMANSKY.

Sarcoidosis Cutis, with Positive Cutaneous Reaction to Kveim Antigen and BCG Vaccine. Presented by DR. MORRIS LEIDER.

E. L., a white housewife aged 39, has been under observation and treatment for the past six months. She presents several waxy to flesh-colored nodules the size of a pea on the back and sides of the neck, telangiectatic macules on the arms and legs and scaly, erythematous patches in the scalp.

Skin tests were performed. Reactions were negative to dilutions of down to 1 : 100 of old tuberculin U. S. P. (old tuberculin Koch). Reactions to tests with Kveim antigens were positive with Copenhagen and Helsinki samples but negative with an Oslo sample.

Reactions to tests with BCG vaccine were positive with live organisms and also with dead organisms.

Serologic tests for syphilis elicited negative reactions.

Roentgenograms of the lungs and bones showed no abnormalities.

Histologic examination confirmed the clinical diagnosis of sarcoidosis.

Considerable improvement was noted after treatment with calciferol (vitamin D_2).

DISCUSSION

DR. LOUIS CHARGIN: In connection with the Kveim test, several points should be borne in mind. First, whether the material is taken from the tonsil, the gland or cutaneous tissue, since the reactions from the various tissues are different. The material taken from the tonsil for the Kveim test gives the strongest reaction of

the three, with that from the gland next, and, finally, that from the skin. Second, I do not think that at this time we are in a position to state definitely, even if the reaction is positive, that we are dealing with a sarcoid process, for in other diseases positive reactions to the Kveim test have been obtained, and in typical cases of sarcoidosis positive reactions have not occurred with active material. In our present state of knowledge one should be cautious in basing a definite diagnosis on the Kveim test alone.

DR. RUDOLF L. BAER: Since the introduction of the Kveim test the observation of reactions to the live and the killed organisms of the BCG vaccine will cause a significant forward step, if confirmed by further studies. A great advantage will have been gained in that a material which is already well standardized, rather than the crude materials heretofore used, will be made available for testing of the skin. The previously employed materials have a number of drawbacks, chiefly that no one batch is identical with another. As a matter of fact, Dr. Danboldt, during his visit in New York, told us that one of the possible reasons that Danish or Finnish investigators noted nonspecific reactions—that is, positive Kveim reactions in some tuberculoderms and some forms of leukemia—was that the Kveim antigen was prepared from tonsil tissue rather than from sarcoid skin or lymph nodes.

DR. ERNEST W. NATHAN: I think Dr. Baer mentioned the essential points, and one can add only some purely hypothetic remarks. I wish to stress one point. So far we have known that anergy is characteristic of sarcoidosis. We learn now that there are certain fractions to which the skin might react with hypersensitive, hyperergic reactions, and only time will enable us to evaluate the significance of these different reactions.

DR. MORRIS LEIDER: In reply to Dr. Chargin's remarks about the reactive accuracy of the Kveim test and the best source of material for production of the antigen, my survey of the literature, including all published material up to 1945, suggests that positive specific reactivity is on the order of 75 per cent. This percentage compares favorably with those for biologic tests of a like nature. The best source for antigen is lymph nodes, except tonsils, affected with sarcoidosis. The tonsils contain so much mixed infection that nonspecific reactions are quite common with antigens prepared from it. The method of preparation is exactly that used by Frei for his antigen in the test for venereal lymphogranuloma.

In a letter recently received, Dr. Putkonen of Helsinki, Finland, who did the largest single series of tests, stated that the Kveim test is quite valuable for diagnosis. There are occasional positive reactions in tuberculosis luposa (lupus vulgaris), lupus miliaris disseminatus faciei and Darier-Roussy sarcoid, but these reactions are weaker than those in sarcoidosis. In any event, some cases of tuberculosis luposa have histologic and other suggestions of sarcoidosis, too, and the other diseases are notable, among other things, for anergy in relation to tuberculin. One may well imagine that tuberculosis luposa may be a tuberculoderm that lends itself to transition into sarcoidosis or is sometimes mixed with an anergic form of tissue reaction.

Dr. Birkhaug of the New York State Department of Health confirmed in correspondence that BCG vaccination with tubercle bacilli in the uninfected person is characterized locally by an incubation period of about two weeks wherein nothing is visible at the site of inoculation and subsequently by the appearance of erythema, nodulation, ulceration and scarring over a period of three to four weeks. In persons who have been infected, there is no incubation period, but rather a reaction time of about twenty-four to forty-eight hours, followed by the rest of the process, which is accelerated and complete in about ten days. Histologically, the first BCG vaccination produces banal inflammation early and tuberculoid structure eventually. After the second inoculation tuberculoid structure appears at once.

Now, what happens when BCG vaccine is given in cases of sarcoidosis, i. e., to persons who are relatively and specifically anergic to tuberculin? We have a clinical demonstration in the case presented. It would seem as if an incubation period appears again, or at least no sure reaction is visible for about seven to ten days. Then a nodule begins to grow. In my patient, the Kveim antigen and the two BCG vaccines, consisting of live and of dead organisms, began to react at about the same time and seem to be keeping pace. Two Scandinavian workers, Lemming and Warfvinge, have had experience with inoculation of tubercle bacilli in cases of sarcoidosis. One used BCG vaccine and the other living, virulent and killed human tubercle bacilli. Both obtained clinical and histologic sarcoids as a result of their injections. I expect to repeat their experiment.

I am hoping that the response to BCG can be developed to become a means of distinguishing sarcoidosis from nonsarcoid tuberculodermas and other unrelated conditions. It ought to be a particularly valuable and safe test in cases of internal sarcoidosis, where biopsy is difficult.

DR. ARTHUR SAYER: Dr. Leider's presentation of the Kveim tests seems to fortify the theory of tuberculous etiology of sarcoidosis. Longcope in America and Pautrier, Besnier and others in Europe have done considerable work on the relationship of sarcoidosis and tuberculosis. These investigators are of the opinion that sarcoidosis is not a tuberculous infection. In fact, they believe that sarcoidosis and tuberculosis are different diseases. Further study of a large series of cases of sarcoidosis with the BCG intradermal tests may settle this important question.

DR. MAX JESSNER: I cannot help but agree with Dr. Leider about sarcoidosis in general, but many more evaluations and examinations will have to be made before definite conclusions can be arrived at. An interesting point, however, is the long incubation period between injection of the material and the start of the reaction. In reference to Dr. Nathan's remarks I should like to state that I do not believe that the sarcoid group can be called absolutely anergic. The idea that sarcoidosis does not show the tuberculin reaction is due to the fact that one does not observe the reaction for a long enough period. In a number of cases the reaction becomes positive the third or fourth day. What the delay is due to we do not know. I have, of course, no proof, but I am inclined to believe that there must be in the Kveim material some tuberculin or some abbau product of tuberculin which accounts for the peculiar reaction.

DR. CHARLES WOLF: In view of the fact that the patient has been under calciferol treatment, would any benefit resulting from it be another link in the chain of evidence that sarcoidosis is a tuberculous disease?

DR. MORRIS LEIDER: With regard to Dr. Wolf's question, I should say that if vitamin D_2 should prove to be a specific for the tuberculodermas, then a favorable response to treatment with it in sarcoidosis would be evidence for a tuberculous relation.

Dr. Jessner stated that in some cases of sarcoidosis the tuberculin reaction is positive after three to four days, which reaction is missed because it is not sought. On the other hand, Jadassohn once said that the reaction in sarcoidosis is missed because it occurs, to use his words, *rasch fertig;* that is, it is over in a flash and therefore not seen. Both these opinions are not in contradiction with the concept of specific positive anergy that is said to obtain in sarcoidosis. In my opinion, the allergization that occurs after exposure to or contact with tubercle bacilli must be conceived as a series of allergic states or as a spectrum of sensitization. A few persons attain exquisite hypersensitivity to the tubercle bacillus and some of its products (tuberculin); most achieve a normergy, i. e., a certain average level of sensitization, and a few reach or become hypoergic or anergic.

Keratosis Follicularis (Darier's Disease). Presented by DR. ADOLPH ROSTENBERG and DR. WILLIAM M. SISKIND.

A. L., aged 36, an American housewife married eighteen years, is the mother of 2 healthy children. The family history disclosed that her mother is living and well. The father died of a stroke. There is no cutaneous disease in the family. The eruption began thirteen years ago during the second pregnancy and was intensely pruritic. It involved the scalp, the temples, the postauricular areas and both sides of the sternum. There were remissions and exacerbations, but the eruption never completely cleared. Treatment included ultraviolet irradiation, roentgen irradiation rays and administration of various medications, both orally and parenterally, without any noticeable effect on the eruption.

The eruption consists of reddish brown, discrete and closely packed papules the size of a pea. The lesions of the scalp form large crusted plaques. Some of the lesions show greasy plugs involving the hair follicles.

Histologic examination by Dr. W. Sachs showed that the epidermis was split in two areas and that the cells manifested varying degrees of hyalinization (corps rond formation). The overlying horny layer was loosely arranged. The microscopic diagnosis was keratosis follicularis (Darier's disease).

The patient received 150,000 units of a preparation containing vitamin A daily for four weeks. The eruption cleared almost entirely. After the treatment was discontinued, a slight recurrence took place.

DISCUSSION

DR. MARTIN BOARDMAN: In a case recently seen at the Skin and Cancer Unit the patient had verruca plana-like lesions on the backs of the hands, which kind of lesions are also present in this patient. In the opinion of Drs. Sulzberger and Jessner, this observation is a part of the picture rather than just an associated phenomenon.

DR. HANS H. BIBERSTEIN: In reference to the verruca plana–like lesions on the dorsa of the hands there is no doubt about the characteristic significance of these lesions. I wish to stress that frequently in keratosis follicularis not only the dorsa of the hands but also the palmar surfaces show verruca plana-like lesions, which are distinguished from similar lesions by the presence of a central point (pores of a sweat gland?). This feature was especially pronounced in this case, as almost all lesions showed the central point.

DR. RUDOLF L. BAER: The speed with which this patient's condition has responded to treatment with oleovitamin A is remarkable. I believe that as a rule it takes much longer for vitamin A to achieve therapeutic results in keratosis follicularis. In the acne cases in which vitamin A therapy appeared to be of some benefit it took in most cases four to six months until improvement was clinically noted. This situation is said to be due to the fact that only a small fraction of the oleovitamin A which the patient takes is actually absorbed. There has been put on the market an emulsified form of vitamin A for oral administration which has been shown to give a high blood plasma vitamin A level much more quickly than the oleovitamin A capsules; with this emulsified form of vitamin A one would expect much speedier results.

DR. MORRIS LEIDER: The lesions on the palms in keratosis follicularis can be visualized more vividly if one takes palm prints. Such a palm print in a case of keratosis follicularis shows clearly the sites of dyskeratoses by distortion of the ridge pattern, particularly on the thenar eminences. Such prints are easy to make by use of an ordinary large size ink pad and absorbent paper. In this case, in

which the condition has shown gratifyingly fast involution under vitamin A therapy and disappointingly fast recurrence on cessation of treatment, it would be interesting to take such prints before resumption of treatment, during treatment and some time after cessation of treatment.

DR. ARTHUR SAYER: It is my impression that patients with keratosis follicularis who show satisfactory clinical improvement with vitamin A therapy have clinical relapses when the use of vitamin A is discontinued. For that reason it is important that these patients continue with their vitamin A therapy in order to maintain their clinical improvement. It can be stated with assurance that prolonged ingestion of vitamin A has no deleterious systemic effects.

DR. FREDERICK REISS: With respect to the therapeutic response of keratosis follicularis to vitamin A, a period of six weeks is a rather short one. In pure vitamin A deficiencies, as observed in China, emulsified vitamin A was not used, but cod liver oil only, and in three to six months excellent results were obtained. In cases of true vitamin A deficiencies the response should be rapid, and in eight weeks an appreciable improvement should be noticed.

DR. RUDOLF L. BAER: The point brought up by Dr. Reiss is important. In discussing keratosis follicularis and acne vulgaris we must bear in mind that these dermatoses are not considered to be basically vitamin A deficiencies. Yet we have learned that in some cases high doses of oleovitamin A (200,000 units daily and more) have a beneficial influence on those dermatoses. When a vitamin is used in such huge doses one can hardly refer to the treatment as vitamin therapy in the orthodox sense, i. e., the supplying of a lacking accessory food factor; rather the vitamin is used as a regular drug.

DR. ADOLPH ROSTENBERG: Regarding the time element, there was an improvement of at least 50 per cent in one week and complete disappearance of the lesions in three to four weeks. Now that treatment with the vitamin has been discontinued for the past three weeks, there is a mild recurrence.

DR. WILLIAM SISKIND: With regard to the speed of improvement, the patients studied by Peck and associates (ARCH DERMAT & SYPH. **48**:17 [July] 1943) were given 150,000 to 200,000 units per day of a preparation containing vitamin A. The papular elements on the body regressed in several months, but the hyperkeratotic lesions on the palms and soles persisted much longer. In our patient all lesions responded rapidly. As Dr. Rostenberg pointed out, the lesions on the palms reappeared when vitamin A therapy was discontinued.

A Case for Diagnosis (Banti's Disease Associated with Purpura? Latent Syphilis?). Presented by DRS. FRANCES PASCHER and DAVID BLOOM.

DISCUSSION

DR. LOUIS CHARGIN: Banti's disease is not a disease. It is a syndrome. It is found in many conditions, even in syphilis. In this condition one encounters vascular disturbances, particularly of the venous system. There is hypertension of the veins, particularly around the spleen, and that is the reason that hemorrhages occur with frequency. There is often a change in the blood, such as leukopenia or low red cell count, and even the white cells are often affected. It is therefore easy to account for the small hemorrhages seen in a patient with Banti's syndrome.

DR. FRANK E. CROSS: The large amount of arsphenamine and bismuth compounds given this patient, who in addition has a history of rheumatic fever, may have been a strong factor in causing so-called Banti's disease.

DR. DAVID BLOOM: A definite diagnosis of Banti's disease has not been made by the medical department of the Post-Graduate Hospital. So-called Banti's disease is associated with thrombopenic purpura, which is not present in this patient. I am inclined to suspect, as Dr. Cross does, the enormous amount of arsphenamine administered to the patient as an important factor in the causation of the illness of the patient—the anemia, leukopenia, hepatomegaly, splenomegaly and purpura.

The main purpose of presenting this patient is the lesion of the ear. The thickened, tender, bluish-discolored rim suggested the diagnosis of pernio, but a diagnosis of purpura was made because of the history obtained and after a general examination of the patient. The dermatologist is likely to be asked to express an opinion in regard to such a lesion, and his acquaintance with such a clinical picture and underlying pathologic factor may help to direct attention early to a general systemic disease.

DR. FRANCES PASCHER: There is no question that the patient has purpura and that we are dealing with a nonthrombopenic type of purpura. The megakaryocytes were well formed and adequate in number. Taking into consideration the normal blood picture and bone marrow studies, we may conclude that the patient has symptomatic purpura secondary to the hepatosplenomegaly. Three possible causative factors for the hepatosplenomegaly have to be considered: (1) rheumatic fever complicated by subacute bacterial endocarditis, (2) tertiary syphilis and (3) toxic hepatosplenomegaly due to arsphenamine and/or bismuth compounds administered over a period of five years.

I agree with Dr. Chargin that Banti's disease is no longer considered a disease entity. Dr. Paul Klemperer, who has made an exhaustive study of splenomegaly, is of the opinion that the term "Banti's disease" will be discarded eventually. So-called Banti's disease, or splenic anemia, may be regarded as a syndrome which may be toxic, hyperplastic or cystic in origin. Correct classification is possible only after clinical and laboratory examination or after splenectomy.

BROOKLYN DERMATOLOGICAL SOCIETY

Abraham Walzer, M.D., *President*

Seymour H. Silvers, M.D., *Secretary*

Feb. 16, 1948

Infection of the Scalp of an Adult Due to Microsporum Audouini Apparently Present Since Childhood. Presented by DR. M. LERNER.

Tuberculosis Indurativa (Bazin). Presented by DR. SEYMOUR H. SILVERS.

Lichen Planus (Hypertrophic); Mycotic Paronychia of Fingers (?). Presented by DR. I. N. HOLTZMAN.

Erythema Multiforme Bullosum. Presented by DR. C. B. LOCASTO.

Moniliasis. Presented by DR. C. T. CHIARAMONTE.

F. H., a white woman aged 60, was admitted to the Kings County Hospital on Aug. 24, 1947, because of a vesiculobullous eruption of seven months' duration involving the face, arms, abdomen, pubis and feet. Prior to admission she had applied many ointments and had received roentgen therapy to the lesions.

There had been a loss of weight of 20 pounds (9 Kg.) during the previous seven months. On admission the patient showed red-crusted, vesicular lesions in circinate arrangement on the extremities, the back of the neck, the thighs and the umbilicus and about the vaginal orifice. Itching and burning has been a major complaint, especially in and about the vagina. From the date of admission to November 1947, the treatment consisted of administration of diphenhydramine (benadryl®) hydrochloride and sulfapyridine and supportive therapy; locally, wet compresses and ointments were applied. In November 1947 a diagnosis of moniliasis was made. During hospitalization, there have been periods of exacerbation and remission of lesions. The lesions at present are on the face, in the axillas and on the vulva and thighs and consist of discrete crusts on a red, ill defined, swollen base.

Results of urinalysis, the serologic test for syphilis and a complete blood count were within normal limits; the reaction of the patch test with iodine was negative. Cultures grown from material taken from the vagina, the anal area and the umbilicus were positive for Candida albicans. Biopsy specimens of the skin taken on two occasions and studied histologically did not add to our information.

DISCUSSION

DR. M. J. CANTOR: I saw the patient one time about four months ago. At that time the lesions resembled those of pemphigus vulgaris.

DR. DAVID M. DAVIDSON: The laboratory observations seem to be in favor of a diagnosis of moniliasis, but I have never seen the disease in such a form. On clinical grounds, I would rather consider the condition a drug eruption. The diagnosis of dermatitis herpetiformis could also be considered.

DR. L. M. FRUCHTBAUM: The clinical appearance and the distribution of the lesions in this case are typical of generalized moniliasis. The laboratory data establish C. albicans as the causative factor. As for therapy, ethyl chloride spray might be tried, but I doubt the efficacy of any local medication; the disease should be attacked systematically, perhaps by iodides.

DR. H. L. FEIGENBAUM: This is a rather bizarre eruption. It does have some of the clinical aspects of fungous infection because of the tendency to spread peripherally, with pronounced elevation of the border. Of course, the cultures and smears showed C. albicans. On the other hand, I have never seen a so-called superficial fungous infection that had as much infiltration or as much induration in the borders as this one does. In addition, I should like to suggest the diagnosis of mycosis fungoides. The amount of infiltration and induration is somewhat suggestive of it.

DR. E. A. GAUVAIN: I cannot agree with any of the diagnoses that have been suggested so far. This is not a solid lesion which is more active in the border and clear in the center, as some have suggested. It is purely an annular lesion. The center of the lesion has not been involved. That situation is not a typical thing in moniliasis, nor in the various mycotic infections. Nor do we find it in mycosis fungoides, where the lesions are infiltrated plaques. My diagnosis is an annular form of impetigo in a debilitated person, possibly with a lowered tolerance of the skin for the ordinary bacteria and, perhaps, with a low vitamin intake. I believe that, with proper nutritional care and simple prophylaxis, such as soap and water and a mild ammoniated mercury ointment, this disorder can be cleared up.

DR. I. N. HOLTZMAN: Histologically, one can rule out several conditions. First of all, dermatitis herpetiformis does not present the picture which this slide showed. The characteristic lesion was an intraepidermic vesicle, which, as Dr. Chiaramonte pointed out, was high up in the epidermis, just below the corneous

layer. These vesicles were filled with numerous cells, most of which were polymorphonuclear. The striking thing about these vesicles was that they were surrounded by flattened squamous cells. There was no edema of the epidermis adjacent to the lesion. This observation indicates that we are dealing probably with a lesion which has infected the epidermis from without and, of course, the two commonest lesions to deal with are fungous infection and pyoderma. In dermatitis herpetiformis, the vesicles or bullae are subepidermic and the entire epidermis is lifted from the corium, as is not the case here. In pemphigus, there is a splitting of the epidermis at the margins of the bullae. There is a perivascular infiltrate in the corium. It is fairly dense and is composed of small round cells and a sprinkling of polymorphonuclear leukocytes. There is, however, not enough polymorphism of the cells themselves to lend support to the diagnosis of mycosis fungoides, but I will admit it cannot be entirely ruled out just on the basis of the histologic evidence. It would seem to me that, with the laboratory findings of C. albicans cultured from the contents of the vesicles and from the rectum, stools, and elsewhere, we certainly are dealing with a form of monilial infection; whether it is secondary cannot be stated. In regard to a therapeutic suggestion, there have been cases reported of extensive cutaneous moniliasis which have responded to treatment with iodides. I think that might be tried. Also, culture for organisms should be taken to rule out a diagnosis of impetigo. I think intensive doses of penicillin and/or iodides might lend therapeutic support to one or another of the diagnoses.

DR. ABRAHAM WALZER: Those patches on the face and across the nose and on the eyelids were destructive lesions. There is atrophy in the center of the spots, and the borders are raised. These lesions are not those of moniliasis. The condition is not pemphigus or impetigo. Nor is it mycosis fungoides, as was suggested, in spite of the fact that the onset of mycosis fungoides could take almost any form, from a simple erythema to eczema or psoriasis. The report of the histologic features does not help. I cannot suggest a diagnosis.

Dermatitis Vegetans of Leg. Presented by DR. C. T. CHIARAMONTE.

Scars Following Impetigo Contagiosa (Ecthyma?). Presented by DR. SEYMOUR H. SILVERS.

A Case for Diagnosis (Frostbite?). Presented by DR. E. A. GAUVAIN.

H. D., a boy 1½ years old, was exposed to the cold on December 26, and both cheeks turned red. About one week later, the affected area was discolored black and blue, the appearance resembling that following a subcutaneous hemorrhage. One week later the patient was hospitalized because of an intestinal infection, at which time hard lumps appeared in each cheek and under the chin.

The patient presents three hard, infiltrated plaques, apparently in the cutis. They are round, sharply limited and about 1 inch (3 cm.) in diameter, with a normal integument. There is no tenderness.

DISCUSSION

DR. DAVID M. DAVIDSON: I do not believe that we are dealing with sarcoid in this case. These lesions are a result of intense cold; friction is probably also a factor, because such lesions are sometimes seen under the chins of children as a result of cold and friction from their winter hats. Histologically, I believe that we should find a foreign body type of reaction due to changes in the fat as a result of cold.

Latent Syphilis and Sarcoidosis. Presented by DR. DAVID M. DAVIDSON.

Gumma of the Chin. Presented by DR. SEYMOUR H. SILVERS.

CLEVELAND DERMATOLOGICAL SOCIETY

George W. Binkley, M.D., *President*

George H. Curtis, M.D., *Secretary*

Gerard A. DeOreo, M.D., *Reporter*

Jan. 22, 1948

Senear-Usher Syndrome (Pemphigus Erythematosus). Presented by DR. H. N. COLE JR. and DR. R. C. LIGHT.

Sturge-Weber Syndrome; Syringocystoma; Polycystic Kidney, Left; Congenital Syphilis, Late. Presented by DR. W. L. MARMELZAT and DR. A. E. WALKER (service of DR. H. N. COLE and DR. J. R. DRIVER).

A Case for Diagnosis (Pityriasis Rubra Pilaris? Multiple Cutaneous Squamous Cell Carcinoma?). Presented by DR. E. W. NETHERTON.

Pemphigus Foliaceus. Presented by DR. W. L. MARMELZAT and DR. A. E. WALKER (service of DR. H. N. COLE and DR. J. R. DRIVER).

Cushing's Syndrome (Pituitary Basophilism) with Atrophic Striae of the Skin in a 3 Year Old Child. Presented by DR. A. E. WALKER and DR. W. L. MARMELZAT (from the Department of Pediatrics, University Hospitals, DR. C. F. MCKHANN, Director).

Epithelioma Adenoides Cysticum with Early Malignant Changes (Cylindroma?). Presented by DR. BENJAMIN LEVINE.

A Case for Diagnosis (Mongolian Spot? Blue Nevus [Jadassohn-Tièche]?) in a White Woman Aged 24. Presented by DR. HAROLD N. COLE JR. and DR. R. C. LIGHT (from the office of DR. H. N. COLE and DR. J. R. DRIVER).

Sarcoidosis. Presented by DR. W. L. MARMELZAT and DR. A. E. WALKER (service of DR. H. N. COLE and DR. J. R. DRIVER).

Tuberculid. Presented by DR. A. E. WALKER and DR. W. L. MARMELZAT for DR. G. BINKLEY and DR. H. JOHNSON.

A Case for Diagnosis (Lichen Scrofulosus?). Presented by DR. W. L. MARMELZAT and DR. A. E. WALKER (service of DR. H. N. COLE and DR. J. R. DRIVER).

A Case for Diagnosis (Parapsoriasis Varioliformis?). Presented by DR. E. C. STERN.

LOS ANGELES DERMATOLOGICAL SOCIETY

Franklin I. Ball, M.D., *President*

Jud R. Scholtz, M.D., *Secretary*

Jan. 13, 1948

Basal Cell Epithelioma (Recurrent). Presented by DR. N. P. ANDERSON.

A Case for Diagnosis (Toxic Erythema?). Presented by DR. RALPH COOMBER, Chicago.

Subungual Petechiae of the Fingers: Dermatophytosis and Onychomycosis (Trichophyton Purpureum). Presented by DR. SAMUEL AYRES JR.

The patient is a white woman who has been under treatment at intervals for nearly ten years because of a fungous infection of the feet with involvement of the nails due to Trichophyton purpureum. The condition has been kept under partial control by various fungicides and by the grinding away of the diseased toe nails.

Three and a half weeks ago, after a manicure, changes consisting of brownish spots and specks beneath the nail were noted in one finger nail. Within a week all the finger nails were similarly involved, and the condition has become progressively more evident. The possible significant factors in the history are that ten days prior to the onset the patient had "intestinal flu" and a tingling sensation in the tips of the fingers and that several weeks before, the patient used a new base coat—everon,® made by Revlon—on the nails.

Examination of the finger nails revealed longitudinal, dark reddish brown to black streaks and dots appearing deep in the nail substance or perhaps in the nail bed, the involvement being predominantly in the distal half of the nails. Microscopic examination of scrapings from the nails revealed numerous red cells but no fungi. There is also a faint, diffuse, brownish discoloration of the entire nail structure. A carefully made hemogram revealed no abnormalities. The bleeding time was found to be 3½ minutes; the clotting time, 3 minutes, and the thrombocyte count, 230,000. The reaction to the Rumpel-Leede tourniquet test was mildly positive.

The patient has received rutorbin® (1 part rutin and 5 parts ascorbic acid), 1 capsule three times daily, for one week.

DISCUSSION

DR. HARRY P. JACOBSON: The patient presents two independent conditions: a mycotic onychia and a paronychia which involves all the toes of both feet. The interesting feature about this involvement is the fact that it is so symmetric and complete in all the toes of both feet. I do not believe that the involvement of the finger nails is a result of a fungous infection. The hemorrhagic appearance of the nails and the onset of this condition after an attack of intestinal influenza suggest the probability of an underlying nutritional factor associated with a capillary fragility. I think that this condition deserves further study directed to the establishment or elimination of a toxic, parasitic and/or metabolic factor responsible for the present condition.

DR. I. A. LEWE: I have a patient with a condition similar to that of Dr. Ayres' patient. The discoloration is more purplish, and associated with it is a decided subungual hyperkeratosis. There is no involvement of the toe nails. This patient

also gives a history of using the same two preparations put on the market by Revlon. Reactions to patch tests with everon,® one of these preparations, were positive on the skin. I had the patient apply this compound to the toe nails for forty-eight hours, with no reaction. Examination and culture of scrapings from the nails revealed no fungi.

DR. J. W. WILSON: Infection with T. purpureum may remain unilateral for many years. I agree with Dr. Jacobson that the condition of the finger nails is not mycotic. I do not believe it is a nutritional disturbance, which would usually manifest itself by Beau's lines growing out from the matrix and not by any trouble at the tip of the nail.

DR. T. H. STERNBERG: It seemed to me that the pigment was in the nails, and I felt that this was confirmed by the fact that the proximal fourth of each nail, representing the amount of growth of the nail since the onset, was clear. The chemical background is perhaps worthy of further study. It has been shown that the application of various chemicals to the nails followed by exposure to sunlight will produce pigment. The patient used several new nail lacquers at about the time this trouble began.

Lupus Vulgaris: Excellent Response to Treatment with Vitamin D_2, 50,000 Units Daily. Presented by DR. FLORALOU KETTENBACH.

Congenital Melanoderma with Subsequent Partial Depigmentation: A Case Observed in a Fourteen Month Old Girl. Presented by DR. SAMUEL AYRES JR.

Maxwell J. Wolff, M.D., *President*

Jud R. Scholtz, M.D., *Secretary*

Feb. 10, 1948

Leprosy. Presented by DRS. M. E. OBERMAYER and P. A. BONAR, San Francisco.

The patient, a Mexican-American student aged 21, had always been well except for having scarlet fever as a child. Both parents were born in the State of Sonora, Mexico, and, except for a six months' visit to that country, the patient had not been out of Southern California. He was inducted into the Army in January 1943. A blood test for syphilis performed at that time was reported to have shown a "doubtful" reacton; the test was, however, not repeated nor was treatment instituted. In June 1943 he noticed that his beard and eyebrows were becoming less heavy. At that time a tender and painful red spot, which later ulcerated, appeared on his right leg; healing was slow and with a deep residual scar. From then on similar lesions have been appearing almost continually on both the upper and the lower extremities. The patient entered an Army hospital in December 1943 and has been under almost continuous hospital care ever since. After his discharge from the Army he was hospitalized at two Veterans Administration Hospitals and one county general hospital. In all these institutions repeated strongly positive reactions to the complement fixation and precipitation tests of the blood were noted, but no clinical evidence of syphilis could be detected. Examination of the ulcers revealed no Treponema pallidum or acid-fast bacilli; microscopic study of the ulcers revealed only the presence of obliterative endarteritis.

In December 1946 the patient entered Birmingham Veterans Administration Hospital, where he remained, with a two weeks' interruption, until the end of 1947, when it was thought advisable for him to be transferred to the Los Angeles

County Hospital, where he is isolated at the present time. Examination on entrance to Birmingham Veterans Administration Hospital revealed approximately the same cutaneous findings as are to be observed at the present time. Numerous angular, purpuric macules of various sizes were present on all extremities, some of which lesions had become replaced by punched-out ulcerations, forming bizarre patterns with their raised, erythematous, granulating borders. New lesions kept appearing while the old ones slowly healed, leaving atrophic scars with peripheral hyperpigmentation. Occlusive dressings seemed to aid their healing. The patient was given two separate courses of penicillin, in total doses of 10,000,000 and 5,000,000 units, respectively, without noticeable effect. While he was in the hospital, appendicitis developed, and the appendix was removed. The patient was discharged from the hospital on Sept. 9, 1947, but he reentered on September 24 because of increasing weakness, fatigue, progression of loss of weight and ulcerations. While he had been afebrile up to that time, his temperature then began to show daily elevations to 101 to 102 F., and his loss of weight became more rapid. Frequently he was nauseated and vomited a greenish mucus. It was then that leprosy was considered in diagnosis, which was established by the findings to be enumerated.

Examination reveals a poorly nourished Mexican man who is chronically ill but in no particular distress. His eyelashes are absent, and the outer two thirds of the eyebrows are sparse. Several small telangiectases can be seen on his neck and trunk. Many atrophic, sharply demarcated scars of irregular sizes and shapes surrounded by zones of hyperpigmentation are present on his arms and legs. Several angular, darkly erythematous, slightly raised purpuric macules are visible on the legs. Only two draining ulcers with irregular contours, one on the right arm and one on the right leg, are present; these exude a slight amount of serosanguinous fluid and are granulating at the base and healing from the periphery. The ulnar, the median and the common peroneal nerves are palpable and enlarged, particularly on the right, and nodular thickenings are also palpable. When the ulnar nerve on the right arm is heavily compressed and rolled beneath one's fingers the patient experiences no sensations of pain or numbness.

The lymph nodes are enlarged and palpable. There is general enlargement of lymph nodes, which can be palpated. The anterior nasal septum is perforated. The liver is palpable 2 cm. below the costal margin. The senses of pain and temperature are lost in the proximal portions of the extremities and completely lost in the distal parts. Tactile sensibility is also impaired in these areas. The reactions to the lepromin (Mitsuda) and the coccidioidin tests were negative; the reaction to the tuberculin test was 2 plus in the first dilution. The reaction to the quantitative Kahn test ranged from 20 to 160 units. Urinalyses consistently demonstrated albumin (1 to 3 plus) and occasional to moderate numbers of white blood cells and red blood cells; tests of kidneys and liver showed decided impairment of function. Examination of the blood gave the following results: red blood cells, 3,000,000 to 4,000,000; hemoglobin, 9 to 12 Gm.; white blood cells, 5,000 to 10,000, with a normal differential count on numerous occasions; and serum albumin, 3.6; globulin, 3.1, and total serum protein, 6.7 Gm. per hundred cubic centimeters. Tests for amyloid, urinary porphyrins, Bence Jones protein, red blood cell fragility and sickle cell anemia were negative; determinations of the basal metabolic rate and examination of spinal fluid showed normal conditions.

Roentgenograms of the chest, the large bones and the kidney, ureter and bladder showed no abnormalities.

Intracutaneous injections of an aqueous solution of histamine, 1:5,000, failed to produce an erythematous flare on involved or apparently normal skin.

Microscopic examination of tissue removed from the nasal septum and from one of the ulcers on the leg revealed the presence of many bundles of acid-fast organisms in the subcutaneous layers. Biopsy of apparently normal skin showed the presence of perivascular focal accumulations of histiocytes, suggestive of leprosy, but no acid-fast organisms could so far be demonstrated.

Treatment during the months of November and December 1947 consisted of intramuscular injections of streptomycin.

DISCUSSION

DR. M. E. OBERMAYER: This is the first case of diffuse lepra leprosy observed in the United States. There is a special form of leprosy reaction which is unique and characteristic for diffuse leprosy. Erythema necroticans, as the cutaneous lesion is called, appears in the form of tender, erythematous, slightly infiltrated macules of an irregular, often triangular, shape; these macules soon become necrotic and often ulcerate, leaving sharply circumscribed, atrophic scars.

DR. L. H. WINER, Beverly Hills, Calif.: In the histologic section there was an irregular, diffuse cellular infiltration of foam cells, and these foam cells, on staining with the Ziehl-Neelsen method, showed numerous organisms.

DR. M. E. OBERMAYER: The advent of the sulfone derivatives, promin® (sodium p,p'diaminodiphenylsulfone-N,N'-didextrose sulfonate) and diasone® (disodium formaldehyde sulfoxylate diaminodiphenylsulfone), seems to have changed the exceedingly poor prognosis of lepromatous leprosy for the better. On my visit to the leprosarium at the Island of Molokai, two months ago, I was impressed by the absence of the typical glossy, copper brownish shade of the lepromatous nodules, which all appeared to be undergoing involution; likewise, the necessity of tracheotomy is becoming less and less frequent when lepromatous patients with lepromatous leprosy are treated by these experimental drugs. Whether the patient with diffuse leprosy will be benefited to the same degree remains to be seen.

Lymphangioma Circumscriptum on the Sacral Area. Presented by Members of the Department of Dermatology, Los Angeles County Hospital.

Deficiency Disease: Glossitis, Cheilitis, Perlèche and Intertrigo (Inguinal) in a 71 Year Old Woman with Diabetes. Presented from the Los Angeles County Hospital.

Blastomycosis of the Foot Treated Successfully by Topical Application of Strong Iodine Solution U. S. P. After Curettement. Presented from the Los Angeles County Hospital.

DISCUSSION

DR. W. J. STEWART, Berkeley, Calif: In several resistant cases of blastomycosis I have used blastomycin administered intravenously, combined with benzoic acid administered by mouth. The method of administration is as follows: Skin tests are made with the blastomycin in varying dilutions and read in twenty-four hours; the greatest dilution which gives a positive reaction to the skin test is used at the beginning of intravenous therapy. For example, if a patient reacted to the dilutions of 1 to 500 and 1 to 1,000 but not to that of 1 to 2,000, treatment would be started with intravenous injections of 0.05 cc. of the 1 to 1,000 dilution. Injections are made three times a week, and the dosage is increased with each injection by 0.05 cc. until the tolerance level is reached. This level usually lies between 0.3 and 0.5 cc. of undiluted antigen. The rate of increase can be determined only by the clinical

response. Increases in temperature and pulse rate, chills and urticarial reactions have been noted. These reactions can be avoided by not exceeding the tolerance level, which varies in different patients.

Benzoic acid is administered by mouth every four hours during the waking hours. The initial dose is 1.0 Gm. This is maintained for about a week, and then the dose is increased to 1.5 Gm., given every four hours. The dose is increased each week until tolerance levels are reached. The drug may be discontinued at any time considered advisable. Reactions to the benzoic acid are similar to those produced by the salicylates.

I am not certain how the benzoic acid works. It is detoxified by the liver. In fact, there is a liver function test based on the ingestion of benzoic acid. Large doses are given so that there is a greater chance of getting benzoic acid into the circulation and thereby carried to all the lesions.

DR. L. H. WINER, Beverly Hills, Calif.: I should like to point out that our technician demonstrated that one of the budding organisms showed possible endospores in blastomycosis. I should like to hear from some mycologically interested contributors regarding this.

Granuloma Annulare, with Dissemination Following Calciferol Therapy. Presented by DR. FLETCHER HALL, Santa Monica.

The patient is an unmarried white medical secretary, 22 years of age. Her family and personal history reveal no evidence of tuberculosis and other possibly relevant conditions.

She first noted two pink, ringlike patches on the flexor aspect of the right wrist in August 1947; at about the same time she noticed that the site of a minor injury to the dorsum of the left foot persisted as a pink, elevated plaque. A few weeks later pink patches appeared on the inner aspect of the lower part of the thighs, and in December 1947 some larger pink plaques appeared on the medial aspect of the middle part of the thighs. Early in January, about two weeks after the patient began to take calciferol (drisdol®; crystalline vitamin D_2 in oil), 50,000 units three times a day, faint pink, ill defined, grouped maculopapules appeared on the anterolateral aspect of the hips, in the groins and on the posterolateral aspect of the buttocks; little if any change in the original lesions was noted during or after calciferol therapy (two weeks). There has been no itching or other subjective complaint. The lesions in the region from which a biopsy specimen was taken on Jan. 27, 1948 (on the inner aspect of the right knee) have disappeared since biopsy; all other lesions have remained relatively unchanged.

Reactions to a tuberculin patch test (Vollmer) were negative; the Eagle and Kline tests of the blood gave negative reactions; observations at biopsy were consistent with a diagnosis of granuloma annulare. Six weekly unfiltered roentgen treatments of 75 r each were given to the wrists and inner aspects of the thighs between Dec. 22, 1947, and Jan. 26, 1948; there has been no treatment since. Caroid® (a digestant preparation obtained from papaya) and ox bile extract U. S. P. (bile salts) had been taken every few weeks during the period of onset, and up to Dec. 22, 1947 (when the patient was first seen by me), no improvement was noted during the next six weeks while no medicine was taken, and no flare-up was noted when this medicine was resumed a week or so ago.

DISCUSSION

DR. M. T. MAYNARD, San Jose, Calif.: For at least fifteen years I have been prescribing calciferol in cases of granuloma annulare; until recently I thought that it probably was the only drug that heals this disease. I continue treatment with

it for six months to a year, with apparent slow healing. The patient may get well anyway. A patient under my care at present, who had a number of rapidly developing lesions and who within a few weeks had many more, was given treatment with drisdol® when she first came in. She is still being treated with it. It has been one year since treatment was started. The lesions have been healing, and the patient is still taking calciferol. I will not say whether or not my patient or the present patient showed an adverse reaction. We cannot deny the possibility that such an occurrence may take place.

DR. JUD R. SCHOLTZ, Pasadena, Calif.: The present patient said that many of the new lesions disappeared and reappeared overnight. The early lesions looked urticarial to me. It is interesting that some people have considered that granuloma annulare is at one extreme and urticaria at the other extreme of the "exudative erythema" group. I doubt that granuloma annulare is as dangerous as calciferol therapy.

DR. FLETCHER HALL, Santa Monica: First, I want to say that the biopsy specimen was taken from one of the new lesions, not from one of the old, clinically typical lesions; the new lesions were the result of dissemination. If there were any who looked at the slide and did not feel that it was typical, the reason may have been that the specimen was from one of the newer lesions. As for the patient's having said that lesions came and went, I believe that she was misunderstood; the lesions do not come and go, but they become more and less obvious. Sometimes they are pale and difficult to see, and on other days they are pink and violaceous. My associates and I have kept careful track of them. With regard to disappearance of the lesions at the site of biopsy, it was my impression that this frequently happens in cases of granuloma annulare; I think that in this case the old lesions, near the new ones which were infiltrated with procaine (novocain®) also disappeared. I believe that if it proves to be true that tuberculous lesions and lesions related to tuberculous etiology tend to flare up after treatment with calciferol, and if this flare-up is due to calciferol therapy, there may be provided some evidence that granuloma annulare is distinctly related to tuberculosis.

Pityriasis Rubra Pilaris, with Improvement After Therapy with Vitamin A. Presented by DR. MAX WOLFF.

Tuberculosis Luposa (Lupus Vulgaris): Improvement After Treatment with Calciferol (Vitamin D_2). Presented by DR. J. WALTER WILSON.

Tuberculosis Verrucosa: Improvement on Treatment with Vitamin D_2. Presented by DR. J. WALTER WILSON.

Poikilodermatomyositis. Presented by HAROLD E. ANDERSON, M.D.

The patient is a 27 year old white American woman of English descent, who is employed as a bookkeeper.

An uncle has tuberculosis; the daughter of her half-sister has diabetes, and her brother has petit mal. The patient had an abscess of the breast about one year ago.

The present eruption began in April 1947 on the face and exposed parts of the arms in such a manner as to suggest the diagnosis of contact dermatitis. I saw the patient for the first time in September 1947, at which time she presented an erythematous, squamous eruption about the eyes, forehead, neck, forearms and buttocks, which eruption, at that time, still had the appearance of a contact derma-

titis. The eruption has been very pruritic, so that, with the patient's excoriations, it had the appearance of atopic dermatitis during November and December 1947. About that time it began to take on the present characteristics, including atrophy, pigmentation, depigmentation and telangiectasia, along with the myositis, so that Dr. Obermayer, in consultation, made the diagnosis of poikilodermatomyositis.

The general appearance is that of a young woman with swelling about the face, apparently in some distress. The eruption consists of an intermingling of telangiectasia, pigmentation, depigmentation, atrophy and scaling, involving the eyelids, the lower part of the face, the neck, the arms and the backs of the hands and the lower part of the trunk and the thighs. There is swelling of the eyelids, and at times there is swelling of muscles, such as the trapezius muscles on the top of the shoulder. The medical history is noncontributory.

A complete blood count was as follows: hemoglobin, 12.8 Gm.; white blood cells, 5,600; red blood cells, 4,200,000; polymorphonuclear leukocytes, 72 per cent; lymphocytes, 21 per cent; monocytes, 5 per cent, and eosinophils, 2 per cent.

Treatment has been of no avail. This has included ten exposures to superficial roentgen therapy of 75 r each during the early stages; injection of calcium gluconate intravenously and of adrenal cortex intramuscularly; soothing local applications, such as aluminum acetate solution N. F. (Burow's solution), wet compresses, calamine lotion N. F., tripelennamine (pyribenzamine®) ointment, phenobarbital and ascorbic acid, 100 mg. twice a day.

DISCUSSION

DR. W. H. GOECKERMAN: This to me was the most interesting case presented today. I rather object to the term poikiloderma in connection with a great many of the various cutaneous disorders. If a reasonably accurate diagnosis can be made, this term is not applied to lupus erythematosus or to radiodermatitis, despite the fact that an occasional case somewhat resembles the poikiloderma of Jacobi. I have followed with much interest the whole question of poikiloderma vasculare atrophicans for more than twenty years. While I have during this time seen many cases which somewhat resembled Jacobi's disease, I have seen only 2 that were typical of Jacobi's disease, and personally I believe that the cutaneous picture is very characteristic. In the case presented today I do not even see a poikiloderma-like eruption, if we use the term in the sense that Jacobi used it, and he was the originator of it. The whole literature on this subject, in my opinion, is very confused although extremely voluminous. If one studies it carefully, it is difficult for one to escape the impression that many of the cases reported do not even resemble the poikiloderma of Jacobi. While the case presented today may belong to the dermatomyositis group, I am more inclined to favor a diagnosis of scleredema adultorum (scleredema of Buschke).

DR. A. V. GRECO, Los Angeles: This patient cannot extend her elbows beyond an angle of about 120 degrees. She can flex the elbows so that she can barely touch her shoulders with her thumbs. There is great muscle weakness and pain in the knees, so that she can walk only with great difficulty. To my mind, the involvement of the muscles and joints brings this case into the class of simple dermatomyositis.

DR. L. H. WINER, Beverly Hills, Calif.: I don't like the name poikiloderma, either, but I cannot agree with Dr. Goeckerman because of the fact that most cases of scleredema adultorum spontaneously clear up and usually involve much of the upper extremities. I have never seen one as extensive as this. I believe this case is an instance of lupus erythematosus. Moving the arms caused pain in the joints.

The histologic picture agrees with that of lupus erythematosus acutus. It shows an intense edema of the cutis. There is a cellular infiltration between the muscle fibers. I agree with the diagnosis as presented.

DR. G. V. KULCHAR, San Francisco: I agree with Dr. Goeckerman that the disorder is a poikiloderma-like reaction. There have been recent reports of poikiloderma-like reactions in neurosyphilis and certainly in dermatomyositis. I think that this woman's condition certainly conforms with the idea that the poikiloderma reaction is more or less a symptom. This eruption is typical of dermatomyositis.

Periarticular Nodes of Rheumatic Origin (?). Presented by DR. M. E. OBERMAYER and DR. E. T. FOX.

Lipoma of the Hand. Presented by DR. SAMUEL AYRES JR.

NEW ENGLAND DERMATOLOGICAL SOCIETY

Francis M. Thurmon, M.D., *President*

G. Marshall Crawford, M.D., *Secretary*

Feb. 11, 1948

Eosinophilic Granuloma of the Skin (?). Presented by DR. G. MARSHALL CRAWFORD, Brookline, Mass.

A. W., a 46 year old white man, is presented with an eruption on his face, of about a year's duration. The first lesions were two small, red, asymptomatic spots on the right cheek, which grew very slowly. They were treated with an "electric needle" by the patient's physician about ten months ago. Growth seemed to stop for a time thereafter, but enlargement again became noticeable six months ago. Since that time two more small lesions have appeared, also on the right cheek. There has been no ulceration, bleeding or crusting at any time. The patient has been under observation for the past six months, and there has been essentially no change in any of the lesions during that time.

The original lesion is situated high on the right malar region. It is a 3 by 5 mm., nonelevated, intradermal plaque. It is a dull shade of red, with a somewhat shiny surface. There is moderately firm consistency to the lesion, but no deep infiltration is palpable. Just to the right of the mouth is the next oldest lesion. This is now only 2 by 4 mm. Two still smaller lesions may be seen just lateral to it. When seen three months ago, all these lesions were elevated from 1 to 2 mm. Since that time they have flattened and a still newer one has appeared on the left malar region. This new lesion is only 2 by 3 by 1 mm. and is not as dark as the others.

A biopsy specimen was removed from the oldest lesion and reported as showing "focal infiltration of inflammatory cells with eosinophils, compatible with eosinophilic granuloma; the picture did not suggest sarcoid." The reaction of the blood in the Hinton test was negative. There has been no treatment.

DISCUSSION

DR. WALTER F. LEVER, Boston: The histologic section from this patient revealed an infiltrate consisting of scattered collections of cells, mostly lymphocytes. There was a moderate number of eosinophils throughout the section, but only a few

histiocytes, and histiocytes are the basic cell in eosinophilic granuloma, with the eosinophils representing a tissue reaction to the histiocytes. Histologically I hesitate to make a diagnosis of eosinophilic granuloma, mainly because there were not many histiocytes. In those cases which my associates and I have called cases of eosinophilic granuloma, histiocytes were much more numerous than in this patient. (Lever, W. F.: Eosinophilic Granuloma of the Skin: Its Relation to Erythema Elevatum Diutinum and Eosinophilic Granuloma of Bone: Report of Case, ARCH. DERMAT. & SYPH. **55**:194 [Feb.] 1947; Lever, W. F.; Lane, C. G.; Downing, J. G., and Spangler, A. S.: Eosinophilic Granuloma of the Skin: Report of Three Cases, ibid. **58**:430 [Oct.] 1948.)

Nodular Nonsuppurative Panniculitis. Presented by DR. JACOB H. SWARTZ and DR. EARL A. GLICKLICH, Boston.

Sarcoidosis, Cutaneous and Pulmonary. Presented by DR. MAURICE M. TOLMAN, Boston.

A Case for Diagnosis (Scleroderma of Toes?). Presented by DR. GEORGE E. MORRIS, Boston.

E. M., a 25 year old white man, is presented with lesions on several toes of the right foot, of four years' duration. This patient was an ex-soldier who had suffered an injury to the right foot in December 1944. The initial treatment consisted of hot soaks and local applications. Thereafter the patient lost several toe nails, and this shedding of nails has been repeated seven times since the alleged trauma. This foot would always swell when the patient stood on his feet for any length of time. In August 1947 an ulcer developed on the top of the second toe and has not healed since that time. A lumbar sympathectomy was performed in November 1947, but healing of the ulcer did not ensue. The patient denied having had roentgen therapy.

The dorsum of the second toe on this man's right foot shows a clean, granulating, ulcerated area of about 1 by 3 cm. This extends from the nail proximally and curves a little onto the outer side of the toe near its junction with the foot. The great toe, the third and fourth toes, and a zone of 2 or 3 cm. of the adjacent dorsal aspect of the foot reveal somewhat tense, whitish skin, with scattered red and purplish macules of 1 to 2 mm.; some of these discolored areas fade under pressure, and some do not. A few telangiectases are also present in this area.

There has been a great profusion of therapy of various sorts in the past. The most recent measure, since the sympathectomy, has consisted of application of a cysteine hydrochloride cream.

DISCUSSION

DR. MAURICE M. TOLMAN, Boston: There was a peculiar spotty pigmentation, present throughout the area, that I couldn't associate with anything in the history. This started with an injury after which the patient was placed under very hot applications, which treatment resulted in large blisters; the applications were so hot that finally he couldn't feel the heat at all. I should like to make a diagnosis of erythema ab igne with traumatization.

DR. MAURICE J. STRAUSS, New Haven, Conn.: I think this condition might be a result of excessive radiation. Dr. Downing told me the patient admitted that he had been examined with a fluoroscope many times.

DR. C. GUY LANE, Boston: I was interested in the number of telangiectatic vessels on the dorsal surfaces of these toes, and so I asked the man about trauma and whether the trauma had been verified by roentgenologic examination. He

said that the foot had been examined roentgenologically twice and after that had been examined with a fluoroscope several times. With that history and the appearance of the skin, with ulceration, telangiectasia and atrophy in mind, one may conclude that this condition could well be postradiation changes accentuated by the heat, or in other words, a radiodermatitis.

DR. FRANCIS M. THURMON, Boston: When questioned, this patient said he had had three ultraviolet treatments and ten infra-red ray treatments in addition to the fluoroscopy. His hands revealed the bluish color and cold feeling, with moisture, which is seen in thromboangiitis obliterans (Buerger's disease). I presume that the sympathectomy relieved the conditions so far as the lower extremities were concerned. Could this disorder be leprous?

DR. GEORGE E. MORRIS, Boston: I think that this might be dermatitis artefacta.

DR. FRANCIS P. MCCARTHY, Boston: In connection with fluoroscopic burns, I saw a patient recently who went to an osteopath who had just purchased a fluoroscopic machine. The patient was sent to me, about a month after the exposure, with three fluoroscopic burns on her back. The lesions developed within ten days, and they were vesiculated areas about 3 or 4 inches (8 or 10 cm.) in diameter. Two healed, but one sloughed and six months later was excised and a graft applied. I believe that in today's case evidence of radiodermatitis would be provided by a deep biopsy specimen, if the lesion is related to this form of treatment.

DR. G. MARSHALL CRAWFORD, Brookline, Mass.: I also considered a diagnosis of dermatitis factitia. The patient does exhibit changes indicating possibility of too much exposure to roentgen ray, but the peculiar outline of the ulcerated area, which also had thickened edges and a granulomatous and somewhat exuberant base, does not fit well with characteristics of postradiation changes. We should find only atrophic changes as radiation sequelae, and not the distinct thickening which is seen around the edges of this ulcer.

DR. GEORGE SCHWARTZ, Malden, Mass.: Could this be carcinoma?

DR. S. J. MESSINA, Boston: I saw this man several months ago while he was a patient at the Veterans Administration Hospital at West Roxbury. All he presented at that time was a dermatitis with a great deal of swelling of the toes and a crusted area. It was nothing like the condition we have seen today. He was hospitalized in the psychoneurotic ward.

DR. ADRIAN SCOLTEN, Portland, Maine: I agree that this man is psychoneurotic, and it is his psychoneurosis that needs treatment. He said he hasn't done an honest day's work since the war. Can that toe be amputated, or is there anything which makes the amputation inadvisable?

DR. JOSEPH BECKER, New London, Conn.: Why not apply a cast if you think the condition is of artificial origin?

DR. ADRIAN SCOLTEN, Portland, Maine: I don't think it is factitial.

DR. GEORGE E. MORRIS, Boston: I think the man came to me because he didn't want the toe to be amputated.

A Case for Diagnosis (Poikiloderma Vasculare Atrophicans?). Presented by DR. G. MARSHALL CRAWFORD, Brookline, Mass.

Syphilis of Skin, Tertiary. Presented by DR. MAURICE M. TOLMAN, Boston, Mass.

Keratosis Follicularis, with Lesions on the Vulva. Presented by DR. G. MARSHALL CRAWFORD, Brookline, Mass., and DR. CHARLES K. WAINGER, Boston.

DISCUSSION

DR. CHARLES K. WAINGER, Boston: Reports of lesions of the mucous membrane in Darier's disease are not unusual. Brünauer (*Acta Dermat. Venereol.* **6**:131 [June] 1925) found oral mucosal lesions described in 20 out of 100 cases of Darier's disease. He describes the lesions on the buccal mucous membrane and on the soft palate as small, polygonal, mosaic-like nodules. These nodules may become confluent and clinically suggest leukoplakia, but they are rougher in appearance. On the hard palate the nodules are often linear, giving a wrinkled appearance to the mucous membrane. On histologic examination the typical picture of Darier's disease was found, including lacunas, corps ronds and grains. In 2 of our 6 cases there were lesions of the mucous membrane corresponding clinically to those described in the literature. In both instances there were lesions on the palate, with roughened mucosa and small yellowish papules. In 1 case there was wrinkling of the mucous membrane of the palate.

Pityriasis Rubra Pilaris. Presented by DR. BERNARD APPEL, Lynn, Mass.

A Case for Diagnosis (Parapsoriasis or Contact Dermatitis?). Presented by DR. ROBERT H. GOLDFARB, Boston.

Hemangioma of Lip. Presented by Dr. GEORGE E. MORRIS, Boston.

D. M., a 13 year old white school girl, is presented with a lesion on the upper lip which has been present all her life. This tumor apparently has not undergone any independent growth but has merely kept pace with the enlargement of the patient's face. At times it has been observed to swell under conditions of stress and strain, but it has otherwise remained entirely asymptomatic.

Most of the right half of this girl's upper lip is enlarged to approximately twice the normal size. The area is purplish beneath the mucous membrane and the vermilion portion of the lip, but the overlying mucous membrane appears normal. There is no abnormal color visible through the exterior cutaneous portion of the lip. The discoloration extends onto the buccal aspect of the lip and thence almost to the alveolar sulcus, with minor nodular irregularities. The entire mass is easily compressible, and most of the color fades easily.

No laboratory procedures have been carried out. No treatment has been administered. The patient is presented primarily for suggestions regarding therapy.

DISCUSSION

DR. JOSEPH MULLER, Worcester, Mass.: I should suggest contact treatment with a radium plaque.

DR. WILLIAM R. HILL JR., Boston: My experience with irradiation has been unsuccessful, but the use of sclerosing solutions, advocated by Dr. Crawford, has been most efficacious.

DR. G. MARSHALL CRAWFORD, Brookline, Mass.: This lesion could be sclerosed satisfactorily by injections. I would disagree with Dr. Muller for two reasons: first, because angiomas of long duration will be relatively radioresistant, and, second, because of the proximity of the dental organs, I should prefer not to use radiation. With the patient at the age of 13, sclerosing treatment would be slow but should be successful if properly carried out. Results cannot be rapidly achieved, but persistence is usually rewarded.

DR. FRANCIS P. MCCARTHY, Boston: The use of radium is contraindicated in treatment of angiomas with large cavernous vessels. I should use it in treatment of lesions with small telangiectatic vessels but not in that of tumors with large ones.

DR. H. BERTRAM ULLIAN, Everett, Mass.: The history is incorrect; development of the lesion followed an injury when the patient was 3 years old.

DR. C. GUY LANE, Boston: There is another contraindication to the use of radiation in treatment of this girl. She has fifty or sixty years ahead of her. I think that radiation of that lesion at the present time cannot be done without some atrophy and that the atrophy will increase as she gets older. I should be much more in favor of the methods Dr. Crawford advocates.

DR. GEORGE E. MORRIS, Boston: How many of these tumors around the face have been given injections? We have had one bad result following injection into a tumor on the face. The angioma became larger and afterward developed more atrophy than we expected. The present lesion is bigger under a Wood's filter than it looks now. I should be afraid to give injections.

DR. MAURICE M. TOLMAN, Boston: Is this tumor growing?

DR. GEORGE E. MORRIS, Boston: It enlarges on hot and cold days.

DR. ADRIAN SCOLTEN, Portland, Maine: Dr. Eugene Traub has treated angiomas by injection but cautioned against this method for facial lesions.

DR. FRANCIS M. THURMON, Boston: I have had excellent results in the use of injection in treatment of facial lesions.

DR. G. MARSHALL CRAWFORD, Brookline, Mass.: In the series of cases of angioma that I recently reported (Injection Therapy for Angiomas, *J. A. M. A.*, **137**:519 [June 5] 1948), there were 283 hemangiomas, of which 79 were located on the face. Five of these were on the lips. In an additional 23 cases, lesions of the mouth, several of which involved the lips, were exhibited. Analysis of results showed that lesions on all parts of the face and in the mouth or other mucous membrane areas did not give quite as satisfactory a response to injection as did those located on other portions of the body. There was no tremendous difference in response, however, and, in general, injection is a satisfactory method of approach. It is less painful to the patient if injection into a lesion can be made through the mucous membrane rather than through the skin. There are numerous reasons why injection therapy about the face is often a more advisable method of treatment than other modalities. If this lesion is growing, that fact is no deterrent, and as a matter of fact it makes injection therapy even more advisable. I should not hesitate to go ahead. At the present time I am employing an invert sugar solution more than anything else. I have used a good deal of sodium citrate and also monoethanolamine oleate, with satisfactory effects.

DR. JOSEPH BECKER, New London, Conn.: I had a patient, 20 years old, who acquired a lesion following the birth of a baby; this tumor grew very rapidly. It was on the buccal mucous membrane and was treated with three injections of sylnasol.® The patient had pain following the first injection (a 5 per cent solution of the sodium salts of certain of the fatty acids of psyllium seed oil, with 2 per cent benzyl alcohol), but the second and third gave no trouble, and the lesion was completely sclerosed.

DR. FRANCIS P. MCCARTHY, Boston: Is there danger of sloughing?

DR. G. MARSHALL CRAWFORD, Brookline, Mass.: There may be sloughing if the solution is placed superficially; otherwise, there is not. Lesions of angiomatous nature occurring in pregnancy will spontaneously recede in about 90 per cent of the cases. Those following trauma respond perfectly satisfactorily to injections.

DR. JOSEPH BECKER, New London, Conn.: Andrews advocated the use of sclerosing solutions and advised injection well under the lesion.

A Case for Diagnosis (Poikiloderma Vasculare Atrophicans?). Presented by DR. LEO KORETSKY, West Medford, Mass.

A Case for Diagnosis (Tinea Corporis or Pityriasis Rubra Pilaris?). Presented by DR. G. MARSHALL CRAWFORD, Brookline, Mass., and DR. CHARLES K. WAINGER, Boston.

Tertiary Syphilis of Skin (?). Presented by DR. WILLIAM R. HILL, Boston.

A Case for Diagnosis (Pityriasis Rubra Pilaris or Lupus Erythematosus?). Presented by DR. LEON BABALIAN, Portland, Maine.

Mycosis Fungoides: Satisfactory Response to Treatment with Urethane. Presented by DR. MAURICE M. TOLMAN, Boston.

PHILADELPHIA DERMATOLOGICAL SOCIETY

Reuben Friedman, M.D., *Chairman*

Douglass A. Decker, M.D., *Secretary*

Jan. 16, 1948

Localized Calcinosis of the Skin Around the Right Knee Joint. Presented by DR. SIGMUND S. GREENBAUM and DR. SIMON KATZ.

Lingua Geographica in a Child. Presented by DR. H. H. PERLMAN and DR. A. BURTON and DR. A. COHEN.

Cutaneous Coccidioidomycosis (Miliary Type). Presented by CAPTAIN W. W. ANDERSON, Phoenixville, Pa.

R. S. J., a white soldier aged 25, well developed and nourished and not acutely ill, presents in the center of the hard palate an erythematous, depressed scarring process covered by a whitish, adherent membrane. At present there is no edema, but periodically there has been pronounced surrounding edema, with tenderness. There are two other white, inconspicuous similar scars near the gum margin. On the left cheek there is a well defined, slightly elevated, purplish, nonulcerated patch of papules, 2 cm. in diameter. There is no atrophy or scarring, but there is moderate infiltration. A similar lesion measuring approximately 3 cm. in diameter is present in the scalp over the central frontal region, near the hairline; there is no scarring or alopecia. There are three smaller lesions on the right side of the neck and the cheek, two of which have been altered partially by excision for biopsy and culture.

The medical examination showed essentially normal conditions; there is no lymphadenopathy.

This patient was in good health until August 1943, when he noted an itching on the roof of his mouth. At this time he found a white, pinpoint lesion at the site of the itching. This gradually increased in size and slowly spread over the entire roof of the mouth and the buccal and faucial mucous membranes. Six months later he noted a papular lesion over the left malar eminence; it gradually enlarged to its present size over an eighteen month period and has remained sta-

tionary for the past two and one half years. During the past three years similar lesions have appeared in the frontal region of the scalp and on the face and neck. The last lesion appeared approximately six months ago. Since March 1946 there have been several acute exacerbations, consisting of edema and tenderness of the mucous membranes of the mouth, fever and general malaise. These usually have subsided in three days.

Urinalysis showed normal values, and reactions in serologic tests for syphilis were negative. A complete blood count and the sedimentation rate were normal. Roentgenograms of the heart and lungs revealed no abnormalities. Normal conditions were seen in roentgenograms of the long bones, pelvis and skull, except for that of the upper portion of the right humerus. This roentgenogram revealed a possible cystic lesion, 1 by 1.5 cm. Mouse inoculation, culture and a complement fixation test made by Dr. C. E. Smith of Stanford University School of Medicine, Stanford University, San Francisco, were positive for Coccidioides immitis in April 1946. A skin test for coccidioidomycosis also had positive results. Biopsy of the lesion over the left malar eminence was made by Drs. Guy and Jacob of Pittsburgh in January 1946. The sections, prepared in Pittsburgh and demonstrated tonight, show a typical tuberculoid type of granuloma of coccidioidomycosis, including typical fungous cells.

The patient has been treated locally with silver nitrate, methyrosaniline chloride (gentian violet), hydrogen peroxide, copper sulfate, tyrothricin and promin® (sodium p,-p'-diaminodiphenylsulfone-N,N' didextrose sulfonate) jelly, without improvement of the oral lesions. Drs. Guy and Jacob during the past year have employed the following types of systemic treatment: (1) ten intramuscular injections of bismuth subsalicylate, (2) ten intramuscular injections of stibophen (fuadin®), (3) forty-eight intravenous injctions of antimony potassium tartrate, (4) oral administration of potassium iodide for two weeks and (5) roentgen irradiation for eight weeks.

DISCUSSION

DR. FRED D. WEIDMAN: I take it that this disease is a new type of coccidioidomycosis. When I first saw this patient I thought he had a case of lupus miliaris disseminatus faciei, and some of these nodules do have a definite apple jelly appearance. Drs. Guy and Jacob's experience was similar. The first time they thought the condition was lichen planus, and the second time there was infiltration and they thought the disorder was lupus vulgaris. Then biopsy declared the diagnosis. Knowing that the patient has coccidioidomycosis, on purely clinical grounds one would be tempted to regard the lesions as ids, but, of course, the presence of fungous cells such as we saw under the microscope effectually disposes of that diagnosis. Those lesions are coccidioidal granulomas of the skin. I am a little doubtful whether all the lesions in the mouth are of coccidioidal nature. Most of the eruption there is extremely superficial, and Dr. Anderson has examined one scraping from the mouth and has not been able to find the micro-organism. There are some infiltrations around the gums, but we have not undertaken to study the deeper tissue of the more infiltrated lesions on the gums. This man has had excellent care; he was taken right under the supervision of Dr. C. E. Smith at Stanford, who stated that mouse inoculation, culture and complement fixation tests were positive for the organism. One might be tempted to try to find an "out" in this case for this very recessive expression of coccidioidomycosis (four and one half years' duration) on the basis that the organism is of decreased virulence. But it is not; Dr. Smith stated that it is the most virulent he and his associates have. I think that this disorder will turn out to be considered a third clinical form of coccidioidal granuloma. I might say that Drs. Guy and Jacob a number of

years ago had a patient in whom the disease was confined to the knee joint, and they cured him with antimony potassium tartrate. Dr. Guy sent me a culture; I injected it into guinea pigs, and in that case the organism was of very low virulence. There is one other record of cure by antimony potassium tartrate that I know of, and that was in the case of a student who worked in my laboratory on coccidioidomycosis one summer and then went back home and discovered an ulcer on the sole, from which he recovered C. immitis. Both of these cases were local ones. We had some hopes for this young soldier, in view of the limited extent of the cutaneous lesions, until the roentgenograms disclosed the lesion in the humerus.

DR. HERMAN BEERMAN: How contagious is this condition?

DR. FRED D. WEIDMAN: That has received a good deal of consideration at the hospital. Is this man a menace to the physicians who stand in front of him and to the patients round about? The position that the California authorities take is that no precautions need be taken other than those that are taken in tuberculosis. The organism appearing in the sputum is not infectious; only that in the stage of chlamydospores is infectious. The conclusion is apparently supported by weight of authority, and the position of Smith and his co-workers is that there is nothing to be feared in the way of transmission of the disease directly from the patient.

Sarcoidosis (Questionable). Presented by CAPTAIN W. W. ANDERSON, Phoenixville, Pa.

Zosteriform Leiomyoma. Presented by CAPTAIN ULLIN W. LEAVELL, Phoenixville, Pa.

J. K. W., a white man aged 31, presents two patches of widely separated, discrete papules. The one is zosteriform and extends over the left sixth and seventh ribs. The second is about the size of one's palm and lies to the left of the midline immediately above the umbilicus. The papules measure up to 4 mm. in diameter. Most of them are flesh colored, but a few are pink or apple-jelly-like. The more lateral ones are frequently elongated, following the lines of cleavage. They are only slightly tender to deep pressure. Three years ago this patient first noticed eight to ten so-called small cysts on the left side of his chest over the sixth and seventh ribs and lying just anterior to the midaxillary line. About six months later he found a group of similar lesions near the midline, left side, above the umbilicus. There has been no itching, pain, discharge or other symptom in connection with the lesions, and he notices them only if something rubs the involved areas. The patient has had headaches as long as he can remember, but they have never been incapacitating. He has had an "allergic rhinitis" for about seven years, and a "tumor" was removed from his nose five years ago. He had a tonsillectomy at the age of 7 years.

In the biopsy specimen there was a noncircumscribed nodule of typical involuntary muscle tissue. The diagnosis was leiomyoma.

DISCUSSION

DR. FRED D. WEIDMAN: I think all of us remember the patient who was shown here from the Philadelphia Naval Hospital about six months ago—a young man with even more extensive and diffuse zosteriform lesions, with whose case, also, biopsy studies were presented. At that time it was pointed out that in the sections it could be seen that the involuntary muscle was definitely the arrectores pilorum. Sometimes the involuntary muscle concerned is that of the blood vessels,

but more often it is the arrectores pilorum. I should not have diagnosed this case clinically, but there was one point, very clearcut in Dr. Gilman's case, which can be barely discerned in the present one, and that was that some of the lesions were long; the individual papules were two or three times as long as they were broad and followed along the lines of cleavage of the skin. I think the term "zosteriform" is not altogether happy. I think it is better for one to refer to a metameric distribution. When one thinks of zoster one thinks of nerves, and one cannot possibly call nerve tissue involuntary muscle tissue. In the final analysis, zoster is a metameric disease; the intercostal nerves are distributed along certain of the metameres and cannot help being metameric. I doubt that these leiomyomas should be classified as true tumors. Certainly when they have zosteriform distribution they are not following the habit of a neoplasm. A neoplasm is characterized by its lawlessness. It is better to call the condition a hamartomatous disease, analogous to vascular nevi which are hamartomatous and not truly neoplastic.

DR. HARVEY BLANK: I saw a patient with this disease who complained that when he shivered in the cold the lesions became painful. After the injection of small doses of methacholine (mecholyl®) chloride near the lesions, the smooth muscle could be stimulated to contract and reproduce the pain. I would therefore suggest that cholinergic drugs be thus used in a clinical test to stimulate these muscle hamartomas derived from the arrectores pilorum. If the patient feels pain, or gives a history of pain on getting "goose flesh," one has a confirmation of the morphologic diagnosis. I do not know whether this situation would exist for lesions derived from the smooth muscle associated with blood vessels.

DR. HERMAN BEERMAN: What has pain to do with hair muscle?

DR. HARVEY BLANK: I have no idea, but the patient to whom I refer says that the lesions are painful.

DR. FRED D. WEIDMAN: The young man to whom I referred told my associates and me that he had pain only on deep pressure.

Sarcoidosis As Observed in the American Negro. Presented by CAPTAIN ULLIN W. LEAVELL, Phoenixville, Pa.

J. M., a Negro aged 24, presents a well demarcated, slightly elevated, verrucous plaque about 1 cm. in diameter involving the entire surface of the inner canthus of the left eye, extending toward the bridge of the nose and also along the margins of the upper and lower eyelids. A similar, smaller, less verrucous plaque lies at the same site on the right eye. There are superficial scarring, induration and partial depigmentation at some sites and hyperpigmentation at others. A slightly elevated, well demarcated, soft, hyperpigmented, flat nodule about 1 by 2 cm. lies on the posterior surface of the left shoulder, and a similar, smaller lesion, on the anterior surface of the right side of the chest. There is a partially depigmented, slightly elevated plaque on the under surface of the foreskin. The medical examination showed normal conditions except for a moderate generalized lymphadenopathy. The spleen is not palpable.

About six months ago this patient exhibited polyuria, polydipsia, polyphagia and drowsiness. These symptoms have been progressive to date. For the past five months he has been moderately constipated, and on occasions he has passed a scanty quantity of bright red blood. There have been no tarry stools or diarrhea. He has had no operations or injuries, and there is no history of tuberculosis, cancer, diabetes, asthma or hay fever in his family.

The disease began two and a half years ago, when the patient noticed a small nodule on his right upper eyelid, near the inner canthus. Similar lesions have appeared since that time, with coalescence to form nodular plaques.

A complete blood count revealed values that were within normal limits. The roentgenograms of the chest and hands showed normal conditions. A study of the gastrointestinal tract revealed no abnormalities. Urinalysis revealed sugar (4 plus). The initial fasting blood sugar was 350 mg. per hundred cubic centimeters. Reactions to the first strength of purified protein derivative of tuberculin were negative; those to the second strength were 4 plus.

Histologic Report.—Finger: The picture was like that of tuberculosis verrucosa cutis, with only one or two granulomas like those of Boeck's sarcoid. The rest of the granulomas were like those of tuberculosis, but there was no caseation.

Right Inner Canthus: This also had a picture like that of tuberculosis verrucosa cutis. The granulomatous infiltrate was definitely that of tuberculosis, i. e., a fairly dense intermixture of epithelioid cells, foreign body giant cells and lymphocytes.

Lymph Node, Right Axilla: There were myriads of sharply outlined tubercles. They were exclusively epithelioid but occurred with many Langhans' giant cells. There was no caseation. Only one or two asteroid bodies were noted. The diagnosis was tuberculosis (but compatible with sarcoidosis as observed in the American Negro).

The diabetes mellitus is well controlled. No treatment has been given for the cutaneous lesion.

DISCUSSION

Dr. Fred D. Weidman: Tuberculosis verrucosa cutis is the histologic diagnosis, and the clinical diagnosis is sarcoidosis as seen in the American Negro. There seems to be a swing away from the idea that the disease is beyond doubt a form of sarcoidosis. Dr. Michelson pointed that up in a recent paper, and Dr. Klauder and I reported an original case before this society many years ago and did not call it sarcoidosis, but "multiple sarcoid-like granulomas of the skin, of undetermined nature." The objections are that very often in these cases observed in Negroes tuberculosis eventually develops. The histologic picture observed in the Negro is not dependable for the establishment of a diagnosis of sarcoidosis. Generally one does not see the typical picture, at least of Boeck's sarcoid. In our patient the lymph nodes from the epitrochlear region were definitely caseous, and in the patient shown tonight there was a strongly positive reaction to the tuberculin test, which observation is very much against the diagnosis of sarcoidosis. I do not think we shall have the answer one way or the other in this patient until animal inoculation tests have been made. The point that I want to bring out is that I do not think that we should accept it as established that this disease observed in the American Negro is the same condition as sarcoidosis, the Besnier-Boeck syndrome.

Dr. Reuben Friedman: How often have members of the society seen lesions of sarcoidosis involving the penis?

Dr. C. C. Thomas: About six months ago there was a Negro in the hospital who had typical sarcoidosis as seen in the American Negro, involving the face, perianal and penile regions. He subsequently died of tuberculous osteomyelitis and miliary tuberculosis. All the sarcoid lesions had disappeared at the time of his death.

Dr. Fred D. Weidman: The histologic picture in the present patient raised the possibility that the cutaneous lesions were the result of inoculation and not necessarily of sarcoid disease. A verrucous surface always makes one think of externally applied tubercle bacilli, and perhaps something that we ought to keep in mind in our future cases is whether or not there is a history of injury to the parts that show the cutaneous lesion.

RESULTS OF ROENTGEN RAY THERAPY IN PATIENTS WITH PEMPHIGUS VULGARIS

Pemphigus Foliaceus. Presented by DR. SIGMUND S. GREENBAUM and DR. SIMON KATZ.

C. H., a white man aged 45, presents universal redness, thickening and scaling. In September 1945 a round, pruritic blister the size of a dime developed on his chest. Within five weeks the condition became generalized but did not itch, although the surrounding skin did. Later the blisters ruptured and the skin peeled. The patient was febrile during his illness, lost weight and became nervous.

The roentgenogram of the chest showed the lungs and heart to be normal. An electrocardiogram was normal. The Wassermann reaction of the blood was negative. A blood count revealed 13.5 Gm. hemoglobin, 1,400 leukocytes, 70 per cent polymorphonuclear leukocytes, 27 per cent lymphocytes and 3 per cent eosinophils. The serum albumin measured 3.3 and the globulin, 2.8 Gm. per hundred cubic centimeters. Urinalysis showed normal values. The basal metabolic rate was +12.

The report on the biopsy specimen taken from the thigh was as follows: The epidermis showed little keratinization. The epithelium was slightly hyperplastic. There were many macrophages loaded with pigment in the corium and a minimal degree of plasma cell infiltration around capillaries and appendages. Pigmentation suggested drug eruption. The pathologic diagnosis was drug eruption (?), diffuse chronic dermatitis.

The patient has been given the following therapy: sulfadiazine, which reduced the temperature to normal; a full course of anticytotoxic serum, with no relief; acetarsone, with no change and potassium permanganate baths and mineral oil.

Pemphigus Foliaceus. Presented by DR. SIGMUND S. GREENBAUM and DR. SIMON KATZ.

In the case of J. A., a Negro aged 54, an eruption of the entire body developed in 1944. The patient was hospitalized, and a diagnosis of mycosis fungoides was made. He received roentgen ray treatment in January and May of 1944. He was well until September 1946, when there was a return of a generalized, itching eruption. He was readmitted in January 1947, and roentgen rays were again administered. The disorder was diagnosed as chronic eczematous dermatitis in March 1947. In June 1947, a diagnosis of neurodermatitis was made on biopsy.

The skin of the entire body is thick, dry, fissured and scaling, and there are scattered patches of secondary infection with crust formation. The scalp hair is absent. The finger nails are gone. Examination of the heart shows a blowing, systolic aortic murmur.

The roentgenogram of the chest showed left ventricular hypertrophy with widening of the aorta. Reactions to serologic tests for syphilis were negative. The prothrombin concentration was 100 per cent. The cholesterol was 127 mg. per hundred cubic centimeters, 56 mg. or 44 per cent of the total cholesterol in the form of esters. The reaction in the cephalin flocculation test was 3 plus, and the serum colloidal gold curve, plus 4. The sedimentation rate was 40 mm. per hour. A complete blood count revealed 60 per cent hemoglobin, 3,500,000 erythrocytes and 12,000 leukocytes, with 74 per cent polymorphonuclear leukocytes and 25 per cent lymphocytes. Bone marrow was normal except for an increase in plasma cells.

The histologic report was that the nodules suggested mycosis fungoides.

Three grams of nitrogen mustard caused slight improvement.

Pemphigus Vulgaris. Presented by DR. SIGMUND S. GREENBAUM and DR. SIMON KATZ.

P. M., an Italian woman aged 72, in September 1947 acquired a fine, rough, red rash over both forearms and the backs of both hands. This soon spread to the arms, legs and trunk. Shortly thereafter blebs developed on the upper parts of the arms bilaterally, spreading to the shoulders, chest, back and finally down the legs, eventually involving the face and scalp, soles and palms. The bullae have persisted to date, and the extensive erosions are causing much pain. There is a loud systolic murmur over the precordium.

The reaction in the cephalin flocculation test was 3 plus, and that in the thymol flocculation test, 4 plus; the thymol turbidity test gave results of 5.5 units (normal, less than 2). The serologic tests for syphilis elicited negative reactions. A blood count revealed 6.8 Gm. hemoglobin and 11,600 leukocytes, with 93 per cent polymorphonuclear leukocytes, 2 per cent lymphocytes and 5 per cent eosinophils.

The patient has been treated with 1 unit of plasma and 1 unit of blood, potassium permanganate soaks and bland ointment.

Pemphigus Vulgaris. Presented by DR. SIGMUND S. GREENBAUM and DR. SIMON KATZ.

A. P., a Negro woman aged 51, about two years ago began to have itching around the rectum and a cutaneous eruption which gradually spread as she scratched it. She was admitted to hospital on April 6, 1946, and a diagnosis of granuloma inguinale was considered. She had a biopsy at that time, with a report of inflammatory papilloma. Since then her condition has grown steadily worse. The lesions have spread until they involve multiple areas over the entire body. There is now little itching. The patient took a dose of a bromide preparation daily. Over the entire body are scattered areas of decidedly thickened, bullous lesions surrounded by areas of denudation, scaling and exudation. There is an area of alopecia in the center of the scalp. The patient has secondary inflammation of the eyes.

An electrocardiogram revealed normal conditions. The reaction in the cephalin flocculation test was 3 plus. The prothrombin concentration was 76 per cent. The proteins were 5.5; the albumin, 2.7, and the globulin, 2.8 mg. per hundred cubic centimeters. A blood count showed 4,300,000 erythrocytes and 7,300 leukocytes, with 56 per cent polymorphonuclear leukocytes, 22 per cent lymphocytes, 1 per cent monocytes and 21 per cent eosinophils. Urinalysis showed a few leukocytes.

The report on biopsy did not give any constructive information.

The patient has been treated with acetarsone, with some improvement.

DISCUSSION ON CASES OF PEMPHIGUS

DR. SIGMUND S. GREENBAUM: Some months ago Macht of Baltimore suggested the use of roentgen irradiation over the liver and spleen in treatment of pemphigus vulgaris. When I came on service recently I found 3 cases of pemphigus vulgaris, 2 cases of pemphigus foliaceus and 1 of dermatitis herpetiformis. I suggested to the members of the department of radiology that they give these patients heavily filtered radiation in full dosage to the liver and spleen. The Italian woman, who was at the point of death and was covered with large blebs and denuded areas, had almost complete clearing in ten or twelve days. One sees the pigmented areas on her skin tonight where there were large lesions, and I

think only a few crusted areas are left. The second patient, the Negro woman, who was also very ill with pemphigus vulgaris, was treated with acetarsone for a short time, with some improvement. We stopped that therapy and gave her roentgen rays directed to the spleen and liver, and she did very well. The third patient, a white man aged 63, had large and small blebs distributed on the trunk and legs and some lesions of an urticarial nature suggesting Duhring's disease rather than pemphigus vulgaris. But many of the bullae appeared on perfectly normal skin, and there were no subjective symptoms. We treated him with irradiation also, and in a few days almost all the lesions had disappeared. At this time, he was given a blood transfusion and a few hours later died, presumably from transfusion shock. The autopsy showed wet lungs, wet brain and acute splenitis and slight anemia of the liver. The liver and the spleen had received about 1,500 r. The patients with exfoliating dermatitis received the same treatment and have shown no particular improvement. I discussed the entire matter with Macht yesterday in Baltimore, and he said that these patients ought to be followed with his Pels-Macht test and that, if the toxic effect on the plant decreases, no more radiation should be given. The radiation he gives is only 60 to 90 r through 2 mm. of copper. The remarkable improvement of the skin in the 2 women and the man who died make it worth while for one to test the effects of high voltage roentgen irradiation to the spleen and to the liver in all cases of pemphigus vulgaris, maybe not in such large dosage as we used, but perhaps in more than that which Macht suggests; perhaps 500, 800 or 1,000 r.

Dr. Carroll S. Wright: While pemphigus is looked on as an incurable disease, I think there are a number of treatments that may at times prove beneficial. In pemphigus foliaceus there is not much to be hoped for. For pemphigus vulgaris, except in Jewish patients, for whom the outlook is not very good, there have been several methods of treatment that have been beneficial. Dr. Schamberg treated a patient with colonic irrigations, and in a short time this patient was out of the hospital, to live for three years. For several weeks I sprayed a patient with a lotion containing a sulfonamide drug, and every lesion healed, but six months later she had a relapse and eventually died. A patient treated with acetarsone has not had a lesion for at least two or three years. How long this situation will last, I do not know. A second patient treated with acetarsone rapidly became worse, and so my associates and I treated her with sulfadiazine; within forty-eight hours she showed improvement, and in two weeks every lesion had healed. A few vesicles still develop, but this patient has shown the most remarkable improvement I have seen. Whether or not the sulfonamide drugs often help these patients, I do not know, but I believe that, while we do not actually cure these persons, there are several methods of treatment that do help for a time and that we should try one after another of the methods we have at our disposal. I believe Dr. Greenbaum's method is another we can use with temporary benefit.

Dr. Thomas Butterworth, Reading, Pa.: I treated 1 patient with pemphigus vulgaris by using roentgen rays as outlined by Macht, without improvement. One patient with pemphigus foliaceus had improvement with naphuride treatment. Two patients with pemphigus foliaceus and 1 with pemphigus vulgaris had remissions of their disorder after massive doses of vitamin D. In addition to giving large doses of vitamin D by mouth, I use a cod liver oil emulsion externally.

Dr. Edward F. Corson: Dr. Ludy had a number of patients with pemphigus whom he treated with vitamin D preparations, recovery resulting in better than 50 per cent of the cases. He also tried convalescent serum. One patient with

pemphigus vulgaris was treated with massive doses of every vitamin except K and P and in two weeks was entirely free of all active lesions. The condition returned, and he was again treated with vitamins. He responded favorably to the medication, as before. He died of an acute episode in about three months, possibly assisted by the massive doses of vitamin D.

DR. REUBEN FRIEDMAN: We have all seen patients with pemphigus in severe form, perhaps even at the point of death, who became miraculously cured for some reason or other. I recall several patients presented before this society who had at some time been given up as incurable and who yet made apparently complete recoveries. Recently such a patient on Dr. Wright's service at the Skin and Cancer Hospital was treated with intravenous injections of plasma from patients with reputedly cured pemphigus, and she made a complete recovery. Within three weeks, however, she suffered a relapse, was readmitted to the hospital and, despite more injections of plasma, died of the disease several weeks later.

DR. SIGMUND S. GREENBAUM: The case that Dr. Wright mentioned as one of pemphigus foliaceus that he saw about fifteen or twenty years ago was in a Negro girl whom I originally saw almost twenty-five years ago with typical pemphigus vulgaris which terminated in pemphigus foliaceus. As to this question of immune serum or convalescent serum (Greenbaum, S. S.: ARCH. DERMAT. & SYPH. **41**:1073 [June] 1940), if pemphigus is a disease of virus or microbial origin in which antibodies are formed, and if one considers using blood from recovered patients, it is important that large amounts be given. In several cases in which my associates and I used blood plasma from cured patients, no results were obtained, perhaps because not enough blood was given for a fair trial of this method. After Dr. Schamberg's result in the case of pemphigus vulgaris (the man who had been under my care for three or four months), I and many others used colonic irrigations, without result. Only in 1 other case did I see so rapid a disappearance of cutaneous lesions as in this one, and that was in a man who was given merbromin (mercurochrome®) intravenously; he later had a relapse, and other patients subsequently were not helped by this drug. However, when 3 patients with pemphigus vulgaris (2 at the point of death) show such rapid cutaneous improvement as these have shown, I think many more patients should be given the benefit of this therapy.

NOTE.—As of Feb. 16, 1948, both patients with pemphigus vulgaris are up and about for short periods, and they feel well. The skin of the Italian woman is almost normal except for some eight to ten crusted erosions in the lower extremities. One large bleb developed on the left thigh during the month. The Negro woman's skin shows decided improvement, but small areas of dermolysis shown by very flat bullae are present on the back; most eroded areas are well or almost so.

Reuben Friedman, M.D., *Chairman*

Douglass A. Decker, M.D., *Secretary*

Feb. 20, 1948

Atrophic Residua on Skin, Symblepharon and Corneal Opacities Resulting from Stevens-Johnson Disease; Rhinophyma of Face. Presented by DR. IRA LEO SCHAMBERG.

J. J. B., a white man aged 27, presents smooth, flat, slightly elevated, pale and atrophic, sharply outlined plaques on the back, particularly the lower part. There are accentuation of the follicular dells and a surrounding band of hyperpigmentation.

On the sides of the neck and the anterior part of the chest atrophic areas are striate and reticulated. There are hyperpigmented, noninflammatory, nonatrophic macules on the thighs, abdomen and penis. The mouth is normal except for a denuded area on the middorsum of the tongue. There is symblepharon of the right upper palpebral conjunctiva to the bulbar conjunctiva and of the left upper palpebral conjunctiva to the upper half of the cornea. The lower half of the right cornea presents diffuse clouding. The left cornea is thickened, irregular and opaque.

On June 10, 1946, the patient was admitted to the Station Hospital at Stuttgart, Germany, because of a left inguinal bubo. A diagnosis of venereal lymphogranuloma was made, and treatment with sulfadiazine and antimony potassium tartrate was instituted. On June 28, edema of the eyelids and conjunctival injection developed, and on June 29 all treatment with drugs was stopped. On June 29 the temperature rose to 104 F. and a generalized, maculopapular, vesicular rash appeared. The temperature remained elevated between 100 and 105 F. until July 23, after which it remained normal. The rash involved the palate and uvula, and no area of the skin was spared. The eyelids were decidedly edematous. A diagnosis of smallpox was considered. On July 3 the vesicles were larger and several had ruptured, forming confluent crusts. By August 12 the corneas were opaque and there was pronounced conjunctival injection. The patient was treated with transfusions of whole blood, calcium gluconate, penicillin, plasma and fluids given intravenously. On September 6, the left cornea was completely opaque and severe symblepharon was present. In the right eye the lower third of the cornea was completely opaque. The patient now has perception of light only.

A complete blood count on July 8, 1946, revealed 72 per cent hemoglobin (11.1 Gm.) and 6,100 leukocytes, of which 13 per cent were stab cells, 52 per cent segmented cells, 30 per cent lymphocytes, 1 per cent monocyte and 4 per cent eosinophils. The total protein was 6.1 Gm. per hundred cubic centimeters, with albumin, 3.3, and globulin, 2.8. The albumin-globulin ratio was 1.2 to 1. On Sept. 23, 1946, the blood urea nitrogen was 19, the blood sugar, 96, the blood chlorides, 460, and the blood cholesterol, 230 mg. per hundred cubic centimeters.

DISCUSSION

DR. BERTRAM SHAFFER: I think this is an important case, largely because the disorder followed the administration of sulfadiazine and antimony potassium tartrate. A large number of cases of the Stevens-Johnson syndrome have been reported, and it is the consensus that this disease is not the result of a reaction to a drug. About a year ago I saw a case which resulted in complete blindness which followed the administration of trimethadione (tridione®).

DR. IRA LEO SCHAMBERG: I was not aware of cicatricial and atrophic residual cutaneous changes such as this man presents.

DR. C. C. THOMAS: Dr. M. K. Hardy and I reported (*J. Am. M. Women's A.* **3**:1 [Jan.] 1948) a series of 5 patients with similar lesions, though not quite so extensive, the disorder following the administration of sulfathiazole in 3 instances and sulfadiazine in 2. One patient was in many respects the counterpart of this man. She had cicatricial lesions of the conjunctiva and scarring in the urethral region which made it impossible for her to urinate spontaneously, so that dilation and catheterization were required. These patients require constant care and watchfulness. Antihistaminic drugs are effective in abating the symptoms of this type of eruption.

CAPTAIN ROBERT L. GILMAN, Medical Corps, United States Navy: I have seen 4 patients, 3 under my care, and these, together with reports of other cases

that I have consulted, all had a preliminary history of drug ingestion of some sort. Since this syndrome usually starts with associated infection of the upper respiratory tract, one would expect the patients to have received a variety of medicines prior to the onset of the more familiar triad of symptoms. Fitzgerald, in the *United States Naval Medical Bulletin* for January 1947, reported the case of a Negro with an extensive bullous eruption that resulted in death. The onset was associated with the ingestion of large amounts of sulfadiazine for an erroneously supposed gonorrheal urethritis. The patient subsequently manifested symptoms suggesting the Stevens-Johnson syndrome. It is conceivable, in view of his widespread general eruption, that, had he lived, he might have shown the scarring that we saw on the patient under discussion. I have used treatment with antihistaminic drugs in my 3 cases, and the response seemed excellent if not specific.

DR. BERTRAM SHAFFER: The changes that occur on the mucous membranes, especially the eyes, are sometimes progressive. The cicatricial process continues to progress for a number of years, so that blindness, urethritis and various sclerosing changes occur after the "cure" of the disease. In spite of the most meticulous care, the changes in the eye do develop. My patient had two private nurses, day and night, irrigating the eyes. However, herniation of the lens through the cornea developed in both eyes.

DR. FRED D. WEIDMAN: My idea of this disease is that it is more like an erythema multiforme, that is, superficial and more or less bilateral and symmetric. The lesions on the present patient were not that. The development of these plaques of fibrosis, I take it, indicates a deep process. When I first looked at the condition I thought of the Schweninger-Buzzi tumors; I wonder whether this case teaches us anything about a possible origin for these tumors. We ought to inquire whether any such cases as have been reported have begun with the Stevens-Johnson syndrome.

Erythroplasia of Queyrat. Presented by DR. M. H. SAMITZ, DR. PRIMO P. MORI and DR. PETER N. HORVATH.

C. P., a Negro aged 78, presents a nickel-sized, erythematous, glistening, elevated plaque on the dorsum of the penis which extends over the frenulum and the corona sulcus, of three years' duration. He has had generalized arteriosclerosis and difficulty in urination since 1940.

A complete blood count and a leukocyte count were within normal limits. The serologic tests for syphilis elicited negative reactions. An electrocardiogram showed a slight ventricular preponderance.

The report on the biopsy specimen was as follows: "Although not quite diagnostic, the changes could be those of erythroplasia of Queyrat."

The patient has been treated with weekly applications of 0.45 to 0.6 Gm. of neoarsphenamine, with pronounced improvement.

DISCUSSION

DR. M. H. SAMITZ: In 1945 the lesion was removed by electrosurgery, but six or eight months later there was a recurrence. We have modified the neoarsphenamine technic, and I should like to have Dr. Mori explain it.

DR. PRIMO P. MORI: The neoarsphenamine is dissolved in 3 cc. of distilled water, and the lesion is soaked in the solution for five minutes by the clock, twice weekly.

DR. REUBEN FRIEDMAN: The glans penis shows areas of depigmentation and mottled areas of purplish discoloration. Does that observation indicate incipient recurrence of the erythroplasia?

DR. M. H. SAMITZ: Yes. I think there is some tendency to recurrence, but we are offering this case to show the ease of treatment with neoarsphenamine applied locally.

DR. MORRIS MARKOWITZ: Arsenical compounds produce pigmentation, but when they are used with ascorbic acid the pigmentation does not occur.

DR. FRED D. WEIDMAN: I should not dare to make a final and unqualified diagnosis of this disease on the basis of sections alone. They show simply the picture of a precancerosis. The cells are the active, hyperplastic type one sees in leukoplakia or senile keratosis, with the lymphocytes below the epidermis. On the report I stated that the histologic picture was compatible with erythroplasia of Queyrat. As to the plasma cells, I think that they must have been incidental.

Premycotic Phase of Mycosis Fungoides? Neurodermatitis? Presented by DR. M. H. SAMITZ, DR. PRIMO P. MORI and DR. PETER N. HORVATH.

Osseous Tuberculosis, Bacterid (?), Miliaria (?) in a Year Old Boy. Presented by DR. M. H. SAMITZ, DR. PRIMO P. MORI and DR. PETER N. HORVATH.

DISCUSSION

DR. M. H. SAMITZ: When first seen, this patient had granulomatous necrotic lesions in the skin and bones. Our first impression was that the disorder was an eosinophilic granuloma. However, on further study and work-up by the department of roentgenology and the pediatrician, we found that the osseous changes were compatible with those of tuberculosis. There was originally a negative reaction to the tuberculin test, which later became strongly positive. A histologic section read by Dr. Weidman indicated a granuloma of tuberculous or syphilitic origin. We assumed it to be tuberculous and treated it with streptomycin, with striking improvement. The only organism recovered was Escherichia coli.

DR. H. H. PERLMAN: The lesion on the finger clinically resembles tuberculous dactylitis, which is sometimes seen in children. Was calciferol used?

DR. M. H. SAMITZ: No.

Reuben Friedman, M.D., *Chairman*

Douglass A. Decker, M.D., *Secretary*

March 19, 1948

A Case for Diagnosis; Erosions on the Tongue. Presented by DR. E. F. CORSON.

A Case for Diagnosis (Ulcers on the Leg—Factitious? Pyoderma Gangrenosum?). Presented by DR. H. A. LUSCOMBE for DR. EDWARD F. CORSON.

Erythroplasia of Queyrat Involving the Glans Penis and the Skin of the Left Ear. Presented by DR. THOMAS BUTTERWORTH, Reading, Pa.

H. R. K., a white man aged 60, presents a dime-sized, moist, velvety red patch on the right side of the glans penis and the foreskin. There is a bright red

superficial ulcer, 1.5 cm. in diameter, on the posterior surface of the upper part of the left ear. The border is slightly infiltrated, and there is a cystic lesion on the mesial edge.

The condition began four years ago on the glans penis, has gradually increased in size and has always been moist. The condition on the left ear began two years ago and was diagnosed lupus erythematosus. It did not respond to gold and bismuth compound injections. Some relief was obtained with boric acid compresses.

The Wassermann reaction of the blood for syphilis was negative six months ago.

DISCUSSION

DR. HERMAN BEERMAN: This man may have erythroplasia of Queyrat on the penis, but I think that the lesion on the ear is carcinomatous.

DR. CLARENCE S. LIVINGOOD: I agree with the presenting diagnosis.

DR. REUBEN FRIEDMAN: There is nothing about the lesion to suggest the diagnosis of erythroplasia of Queyrat except that it has been present for four years. Perhaps the diagnosis of erythroplasia can be made only by exclusion, because we cannot think of anything else that would be more adequately diagnostic.

DR. IRA L. SCHAMBERG: The man had a few lesions of psoriasis on his face.

DR. ISADORE ZUGERMAN: The patient stated that the lesion on the ear started as a patch of psoriasis, and the lesion on the penis may be psoriasis. I suggest that a biopsy be done.

DR. REUBEN FRIEDMAN: The lesion on his penis is consistent with the diagnosis of Sulzberger-Garbe disease.

DR. HERMAN BEERMAN: Savatard described psoriasiform carcinoma of the penis which is similar to this and looks like erythroplasia of Queyrat. I think that this is psoriasis.

(NOTE.—The biopsy studies were made by Dr. Weidman. He reported mixed basal and squamous carcinoma on the ear and squamous cell carcinoma on the penis. The patient died of coronary occlusion several weeks after presentation.)

Dermatitis Herpetiformis? Erythema Annulare Centrifugum? Erythema Gyratum Perstans? Presented by DR. ARTHUR PRATT.

Schamberg's Disease? Purpura? Presented by DR. G. KNOLL for DR. E. F. CORSON.

Epidermodysplasia Verruciformis. Presented by DR. EDWARD F. CORSON.

F. P., a white boy aged 5 years, presents on the hands, forearms and ears papules which vary in size from that of a pinhead to that of a pea and are flat and rounded or polygonal in outline. The eruption appeared when he was 1 year old, and it resembled warts and was itchy. The lesions increased in number until, in October 1947, there were about forty on each hand, twenty on the forehead and six to eight on each ear. The biopsy specimen, while not typical of epidermodysplasia verruciformis in the opinion of some consultants, was felt by others to show evidence of that condition.

Mercury with chalk, ¼ grain (16 mg.) daily, caused decided improvement, but the condition is now recurring.

DISCUSSION

DR. D. M. SIDLICK: This is lichen planus, except for the absence of violaceous color, a clinical feature which, however, need not always be present.

DR. H. H. PERLMAN: I agree with Dr. Sidlick.

DR. J. M. SCHILDKRAUT, Trenton, N. J.: I think that this is epidermodysplasia verruciformis.

DR. HARVEY BLANK (by invitation): Lutz (*Dermatologica* **92**:30, 1946), in a follow-up of the original patients described by Lewandowsky, stated that their disease followed the course of verruca plana. Lesions were ground up and passed through a filter, and a filtrable agent was demonstrated on inoculation into normal skin. This is, therefore, an unusual form of verruca plana.

Sporotrichosis; Psoriasis. Presented by DR. LESLIE NICHOLAS and DR. BERTRAM SHAFFER.

R. L. G., a white woman aged 38 years, presents on the dorsum of the left hand two crusted infiltrated inflammatory plaques, each approximately 1 by 2 cm. On removal of the crust, pus can be expressed from many sinuses. On the radial aspect of the left forearm there is a 1 cm. subcutaneous nodule, violaceous in hue and soft to the touch, adherent to the skin. After observation for one week, this nodule broke through the cutaneous surface, discharged gray-white pus and became crusted. On each elbow and knee there is an erythematous plaque with silvery white imbricated scale.

In December 1947, the patient noticed a "pimple" on the dorsum of the left hand. This became larger and crusted. Then a similar lesion developed about 1 cm. from the first, and after a few weeks a "boil-like" lesion developed on the radial side of the left forearm. There is no history of ingestion of drugs. She has not handled shrubs with thorns, flowers or raw vegetables. Her last trip out of the city was in the summer of 1947. There is no adenopathy.

Roentgenograms of the chest showed some increase in the prominence of the right hilar shadow and of the bronchovesicular markings in the lower lobe of the right lung. The Kolmer-Wassermann and the Kline reactions were negative. Results of a urinalysis were within normal limits. A complete blood cell count showed 14.5 Gm. hemoglobin, 7,500 leukocytes, 59 per cent polymorphonuclear leukocytes, 1 per cent eosinophils, 37 per cent lymphocytes and 3 per cent monocytes. Culture on bacterial medium produced hemolytic Staphylococcus aureus; on Sabouraud medium, Sporotrichum schenkii. Direct examination of pus (potassium hydroxide preparation) did not reveal fungi.

The report on the biopsy was: There was a moderate pseudoepitheliomatous hyperplasia of the epidermis. There were numerous intradermal and intraepidermal abscesses; the former were surrounded in loci by some epithelioid cells and giant cells. There were no organisms seen in either the abscesses or the infiltrate. The blood vessels were not unusual.

The patient has been treated with saturated aqueous solution of potassium iodide, in increasing dosage, at present 40 drops three times daily, and low voltage roentgen rays, two treatments of 81 r each to each area.

DISCUSSION

DR. LESLIE NICHOLAS: We presented the case because of the unusual histologic picture. The histopathologist made the diagnosis of blastomycosis, although organisms could not be identified. It was only after the culture was done and we

isolated the organism that we were sure that we were not dealing with blastomycosis. This is similar to the verrucous form of sporotrichosis described by Dr. Smith and Dr. Garrett. (Verrucous Sporotrichosis, ARCH. DERMAT. & SYPH. **56**:532-534 [Oct.] 1947.)

SAN FRANCISCO DERMATOLOGICAL SOCIETY

Frederick G. Novy Jr., M.D., *President*

Frances M. Keddie, M.D., *Secretary-Treasurer*

Jan. 16, 1948

Xeroderma Pigmentosa. Presented by DR. FRANCES A. TORREY.

R. H., a 24 month old girl, has had increasing pigmentation and a dry skin since birth.

On her face there are scattered pigmented areas, atrophy, early angiomas and two epitheliomas, located on the right temple and the right nasolabial fold. She also has hyperpigmentation on the neck and the upper part of the trunk. The legs are dry and somewhat erythematous. The epitheliomas are to be treated with radioactive phosphorus.

A protective sun cream containing 5 per cent menthyl salicylate, vitamin A (25,000 units) daily and advice about avoiding sunshine have been given.

D. H., aged 11 months, the sister of this patient, has an abnormally dry skin with a great number of ephelides.

Nevoxanthoendothelioma? Juvenile Xanthoma? Presented by DR. LEO M. COLUMBUS, Berkeley, Calif.

Multiple Benign Cystic Epithelioma. Presented by DR. GRANT MORROW.

Porokeratosis (Mibelli). Presented by DR. EDWARD J. RINGROSE and DR. F. B. NOWLAN.

A. L. S., a 19 year old white seaman, presents the history of a lesion on the dorsa of the fourth and fifth fingers of the left hand. The lesion has been present since the patient was 5 years old and has produced no symptoms. There has been no extension, but the lesion has seemed to increase in size in pace with the patient's growth.

Overlying the bases of the left fourth and fifth fingers and the adjacent portion of the dorsum of the hand is an annular, papular, slightly erythematous lesion. The skin within the border is moderately atrophic. The summit of the border has a fine keratotic ridge surmounting a keratotic palisade. The patient has previously had electrodesiccation and the application of caustics to the lesion.

Cutaneous Diphtheria. Presented by DR. FREDERICK G. NOVY JR., Oakland, Calif., and LIEUT. COL. R. M. WILLIAMS, Medical Corps, United States Army.

R. D., a 25 year old soldier, was admitted to Letterman General Hospital on Dec. 30, 1947, from the Station Hospital, Hamilton Field, Calif., for an undiagnosed condition manifested by chronic ulcers of the right foot and leg, the left popliteal

space and the buttocks. The onset of illness was in mid-November 1947. The previous treatment consisted of local applications and compresses and penicillin therapy for four days. It was discontinued because of generalized rash which was believed to be due to penicillin.

The ulcers varied from about 1 to 3 cm. in diameter and were sharply marginated, with underlying edges; a black eschar covered the bases. A narrow margin of erythema surrounded the margin of the ulcers.

The hemogram was as follows: white blood cells, 13,300; hemoglobin, 13.5 Gm., neutrophils, 63 per cent; lymphocytes, 30 per cent; monocytes, 5 per cent, and eosinophils, 2 per cent. The sedimentation rate was 20. Urinalysis revealed normal values.

The cultures for the isolation of organisms revealed the following: Corynebacterium diphtheriae, two strains of diphtheroids and hemolytic Staphylococcus aureus. The fermentation reactions for glucose and sucrose were positive for strain 1 and negative for strain 2 of the diphtheroids.

Guinea pig 1, protected with antidiphtheria serum, inoculated with 0.5 cc. of saline washings from the culture of C. diphtheriae, showed no reaction. In guinea pig 2, not protected, an erythematous mass, which abscessed but did not rupture, developed. Aspirations from this were cultured, and C. diphtheriae was identified, morphologically and by fermentation.

The sensitivity tests to streptomycin, penicillin and sulfonamide compounds showed the staphylococcus strain to be resistant to penicillin and sulfonamide drugs but sensitive to streptomycin.

On Jan. 4, 1948, the patient was given 50,000 units of antidiphtheria serum; on January 6, 30,000 units. Symptomatic relief of pain followed the first dose of serum within a few hours.

DISCUSSION

DR. ROBERT C. LOFGREN: I saw this patient before treatment was instituted, and I thought there was some black slough in the lesion which suggested diphtheria of the skin. The appearance of the ulcerations also suggested the possibility of infection with microaerophilic or mixed organisms. There is a possibility some secondary infection has prevented more rapid healing. Urticaria from the penicillin has been this patient's only reaction to penicillin. It is my impression that this in itself should not be a contraindication to further use of penicillin.

LIEUT. COL. R. M. WILLIAMS, M.C., U. S. A.: Complete bacteriologic studies were done in this case, and, in addition to C. diphtheriae, two strains of diphtheroids and a Staph. aureus were isolated. There were no microaerophilic or anaerobic organisms isolated. The Staph. aureus was resistant to penicillin and the sulfonamide drugs, but was sensitive to streptomycin.

DR. FREDERICK G. NOVY JR., Oakland, Calif.: At one time the patient had a black, tenacious slough, which is not present tonight.

DR. REES B. REES: Injections of diphtheria toxin-antitoxin mixture might be logical in case he acquires a sensitivity to horse serum before he is well.

LIEUT. COL. R. M. WILLIAMS, M.C., U. S. A.: I spoke to Major Kennedy, who saw several cases of cutaneous diphtheria during the war, and he says that it was quite characteristic for the pain to be relieved within a few hours following administration of the antitoxin.

DR. FREDERICK G. NOVY JR., Oakland, Calif.: The ulcer was much deeper when we saw the patient on the original examination.

Dermatomyositis. Presented by DR. HARRY E. ALDERSON and DR. CHARLES ALBERT SHUMATE.

I. G., a girl aged 9, three months previously had noticed tightness in her right forearm and some itching. Red macules developed on her right arm and later on the dorsum of her right foot. Gradually the skin in these areas became hard, dry and atrophied. Scleroderma-like areas were found. Movement became painful. A red area, showing atrophy, has developed on the right shoulder, and depigmented areas are seen on the upper part of her back.

The urine showed no sugar or albumin. Examination of the blood showed a hemoglobin content of 12 Gm.; erythrocytes, 4,450,000, and leukocytes, 6,000, with a normal differential count. The sedimentation rate was 2 mm. per hour.

Roentgenologic examination of the right upper extremity and the right foot showed the bony components to be normal.

Drs. Wilbert and Perry Sachs, of New York city, in a report on sections taken from the right arm, stated: "The epidermis and the cutis down to the fat showed no important change. The muscle below the fat area had considerable infiltration of small round and plasma cells. The vessels were dilated and filled with blood elements. There were some areas of basophilic degeneration. The diagnosis was dermatomyositis."

DISCUSSION

DR. ROBERT A. STEWART, Berkeley, Calif.: I think that this particular case is one of scleroderma rather than of dermatomyositis.

DR. ERVIN EPSTEIN, Oakland, Calif.: Ten years ago Dr. Ayres and I demonstrated that 7 cases of generalized or localized scleroderma showed creatinuria suggesting muscle involvement (Epstein, E., and Ayres, S., Jr.: Creatinuria in Scleroderma, *J. Lab. & Clin. Med.* **22**:697 [April] 1937). One also sees true cases of dermatomyositis, such as the one that I presented at the previous meeting of this society, in which the cutaneous lesions resemble those of scleroderma. Scleroderma, dermatomyositis, acute disseminated lupus erythematosus and periarteritis nodosa can all be classified under the heading "angiitis." In this case, the clinical picture is certainly that of scleroderma, but the histopathologic picture is that of dermatomyositis.

DR. CHARLES W. MCNITT, Reno, Nev.: I agree that scleroderma and dermatomyositis are difficult to differentiate. It is generally pointed out that there is a relation between acrosclerosis, dermatomyositis and diffuse scleroderma. Certainly, this girl's right hand shows typical acrosclerosis. The macules on the shoulder are depigmented, exhibiting a form of morphea. The skin is of such nature that I should say it could not possibly show "epithelium and cutis essentially normal," as reported by the pathologist.

DR. REES B. REES: Whether there are any muscle changes or not, in the circumstances I think the condition is scleroderma, of the type the neurologists would call abortive hemiatrophy.

DR. EDWARD J. RINGROSE, Berkeley, Calif.: The lesions should be differentiated. Those seen today do not resemble dermatomyositis but, rather, look

like linear scleroderma. The confusion in diagnosis usually arises between dermatomyositis and disseminated lupus, rather than between dermatomyositis and scleroderma.

DR. HARRY E. ALDERSON: Clinically, the appearances are in favor of scleroderma. However, the report that Dr. Sachs made seems to decide the matter. The child has never been ill, so far as I know. She looks well and feels fine. There was a rather large piece of tissue removed, and Dr. Sachs had plenty of material for study; hence we should accept his diagnosis of dermatomyositis.

DR. CHARLES A. SHUMATE: When the patient was first seen scleroderma seemed to be the most likely diagnosis. Further studies and the pathologic report of Dr. Sachs appeared to establish the diagnosis of dermatomyositis. I agree with Dr. Ervin Epstein that there is overlapping between scleroderma and dermatomyositis.

News and Comment

GENERAL NEWS

Exhibits and Motion Pictures at San Francisco Session of the American Medical Association.—Space will be available for Scientific Exhibits and for places on the motion picture program at the San Francisco session of the American Medical Association, June 26 to 30, 1950. Applications should be forwarded immediately to Dr. Francis W. Lynch, 1466 Lowry Medical Arts Building, St. Paul 2, Minn.

Specialists Certified by the American Board of Dermatology and Syphilology.—At the meeting of the American Board of Dermatology and Syphilology in Cincinnati Oct. 21 to 23, 1949, the following 28 candidates were voted certificates and may now be referred to as certified specialists: John W. Albrittain, Long Beach, Calif.; Saul S. Berger, Winnipeg, Manitoba, Canada; John W. Carney, Los Angeles; Fred F. Feldman, Los Angeles; Milton D. Feldman, Dayton, Ohio; Hanes M. Fowler, Dallas, Texas; Walter G. Gasner, Mount Vernon, N. Y.; Bernard G. Geuting, St. Albans, N. Y.; Walter S. Green, Glendale, Calif.; Harold G. Hurst, Winnipeg, Manitoba, Canada; Lewis W. Kirkman, Ann Arbor, Mich.; George M. Knoll, Bethlehem, Pa.; Rene Leviticus, New York; Harry Levitt, Watertown, N. Y.; Robert E. Lloyd, Ann Arbor, Mich.; Herbert A. Luscombe, Havertown, Pa.; Martin G. Marmon, New York; Myles P. Moursund, Glenside, Pa.; Thomas W. Murrell Jr., Richmond, Va.; Raymond A. Osbourn, Washington, D. C.; Norbert G. Rausch, Buffalo, N. Y.; Thomas L. Shields, Fort Worth, Texas; John B. Squires, Cincinnati; Frederick G. Tice Jr., Pueblo, Colo.; Howard H. Volan, Syracuse, N. Y.; Louis Wexler, New York; Kurt Wiener, Milwaukee, Wis., and Victor H. Witten, New York.

The following candidates were also successful in the examinations and will become certified specialists when they have fulfilled the requirement of five years of training and experience in the specialty: James R. Allen, San Francisco; Ralph T. Behling, Burlingame, Calif.; Benjamin Bender, Brooklyn; Henry R. Corwin, New York; David D. Dexter, West Hempstead, N. Y.; Anthony N. Domonkos, New York; Harry M. Eil, New York; Edmund F. Finnerty Jr., Waban, Mass.; Irving M. Fishman, Jamaica, N. Y.; Robert H. Grekin, Kalamazoo, Mich.; Robert D. Griesemer, Boston; Edwin M. Hamlin, San Francisco; Peter N. Horvath, Philadelphia; Stanley E. Huff, St. Paul; Otis F. Jillson, Portland, Me.; Herbert L. Joseph, Vallejo, Calif.; Jerome J. Kaufman, Brooklyn; Arthur B. Kern, Amityville, N. Y.; George H. Kostant, New York; Morton Kulick, New York; Chester M. Lessenden Jr., Bremerton, Wash.; Harry Levitt, Los Angeles; Willard L. Marmelzat, Los Angeles; Louis G. McGoldrick, Worcester, Mass.; Otis B. Miller, Cedarhurst, N. Y.; Donald C. Montgomery, Billings Bridge, Ontario, Canada; Roberts B. Pappenfort Jr., New York; Charles F. Post, Haledon, N. J.;

Samuel J. Randall Jr., Rochester, Minn.; Louis Rubin, Chicago; Socorro A. Simuangco, New York; Otto C. Stegmaier Jr., Davenport, Iowa; Raymond R. Suskind, Cincinnati; Robert F. Tilley, Brookline, Mass.; Alfred Trosow, Philadelphia; George A. Waldriff, Albuquerque, N. M.; George T. Wilson, Palo Alto, Calif., and Murray C. Zimmerman, Whittier, Calif.

Hygeia to Be Renamed.—The trustees of the American Medical Association have authorized the renaming of the Association's health magazine, *Hygeia.* The new name will be *Today's Health,* and the change will be made with the issue of March 1950.

Book Reviews

Der Morbus Besnier-Boeck-Schaumann: Chronische epitheloidzellige Retikuloendotheliose oder Granulomatose. By Stefan J. Leitner, M.D. Price, 38 francs. Pp. 248. Benno Schwabe Klosterberg 27, Basel 10, Switzerland, 1949.

Sarcoidosis has been known for fifty years but has attracted much more attention in the past ten years. The literature consisted largely of isolated articles until Kissmeyer in 1932 published the first monograph on the subject. This was followed by a comprehensive report by Pautrier in 1940.

Leitner published the first edition of his book in 1942. It was an admirable collection of the known facts about sarcoidosis. He proposed the name "chronic epithelioid-celled reticuloendotheliosis or granuloma," basing this title on the well known and consistent histologic picture of lesions regardless of the tissue involved. In the present edition he has brought the literature up to date and added the follow-up observations which he has made on his rather extensive material. This reviewer has stated before that physicians engaged in the study of tuberculosis were best able to evaluate sarcoidosis. Leitner, as chief of the noted Bernese tuberculosis sanatorium in Leysin, Switzerland, has therefore been in a most favorable position to study the disease.

The book is divided into thirteen parts, beginning with a historical account of the disease, a review of the nomenclature and a summing-up of the syndrome as a whole, followed by more detailed discussions of subjects including the pathology, clinical picture and chemistry.

The controversial subject of the etiology of sarcoidosis is ably handled and carefully analyzed. Leitner favors tuberculosis as the cause and believes an altered allergy or euergy (positive hypergy) may explain some of the controversial findings which make tuberculosis difficult to prove.

The book is admirable in every way. There is scarcely a fact pertaining to sarcoidosis which is not covered both by adequate references and by personal opinion. It is hoped that the book will be translated into English. No one interested in the subject can afford to be without a copy.

The only adverse criticism might be notation of the fact that sarcoidosis in the American Negro is not given much consideration, a fact which is readily understandable because of the residence of the author. Also, in the discussion of therapy, nitrogen mustards, which have been used here, are not mentioned.

The Benno Schwabe firm has done, as always, an excellent job of printing.

An Introduction to Medical Mycology. By George M. Lewis, M.D., and Mary E. Hopper, M.S. Third edition. Price, $7.50. Pp. 366, with 103 illustrations. The Year Book Publishers, Inc., 304 South Dearborn Street, Chicago 4, 1948.

This is a valuable book which deals with the clinical, theoretic, experimental and laboratory aspects of medical mycology. Both the superficial and the deep mycoses are fully discussed. The clinical aspect of mycology is especially emphasized and described in considerable detail. The book is easily read and has numerous excellent photographs. It contains many pertinent references. The paper is of fine quality, and the book is well bound.

Classification and terminology might have been considered more fully because of the numerous confusing names which have been and are being used in mycology. For example, the authors use the name "Trichophyton gypseum" instead of

"Trichophyton mentagrophytes," "Microsporum lanosum" instead of "Microsporum canis" and "Epidermophyton inguinale" instead of "Epidermophyton floccosum." The laboratory aspect of mycology could be presented more completely. Common contaminants are dealt with very briefly. More colored photographs of typical cultures would add greatly to the value of the book but, unfortunately, to the price as well.

No dermatologic library would be complete without this excellent contribution to medical mycology.

Excerpta Medica, Section XIII: Dermatology and Venereology. Edited by M. W. Woerderman, M.D.; A. P. H. DeKleyn, M.D., and W. P. C. Zeeman, M.D., all of the University of Amsterdam. Subscription rate, $25 per year. G. J. Thieme, Nijmegen, 111 Kalverstraat, Amsterdam C., The Netherlands.

Excerpta Medica is the collective title for a series of monthly journals of medical abstracts covering the fields of clinical and experimental medicine. It is a nonprofit enterprise sanctioned by the Government of the Kingdom of the Netherlands but dependent on its subscribers for its existence. There are fifteen sections, of which Section XIII is limited to Dermatology and Venereology. The abstracts are written in English, and each abstract is signed. The subscription rate for Section XIII is $25 per year for twelve issues, including an index, classified by author and subject, to be sent on the completion of each volume.

The abstracts are pithy, comprehensive, punctual and well written. Articles, such as case reports, which do not present a significant observation or new therapeutic approach, are listed by title only.

The service is highly recommended to all who are interested in dermatology and venereology.

Syphilis: Its Course and Management. By Evan W. Thomas, M.D., Professor of Clinical Medicine, New York University College of Medicine; Director, Rapid Treatment Center and Visiting Physician, Bellevue Hospital, New York; Consultant, United States Public Health Service. Price, $5.50. Pp. 317. The Macmillan Company, 60 Fifth Avenue, New York 11, 1949.

This book is a report of the experiences of the Bellevue Hospital group of New York city in the treatment of syphilis. It is essentially a survey of the results of treatment thus far obtained from the use of antibiotics for the person with syphilis, so that accordingly some of the observations recorded will need confirmation by treatment and observation of larger series of cases. The deductions in regard to the high incidence of reinfections may be influenced somewhat by the fact that the majority of the patients treated in the clinic were Negroes. The defense mechanism of the patient receives little consideration from the author, as he tends to explain the failures of treatment by offering the strain of the organism, the dosage of penicillin and the time factors as the more likely reasons for the unsuccessful results. Enthusiasm for penicillin in the treatment of the person with neurosyphilis is tempered somewhat by the suggestion that fever therapy should be employed when neurosyphilis is resistant to penicillin.

The book contains few illustrations. It is not encumbered with irrelevant references, and, although displaying a great enthusiasm for penicillin in the treatment of syphilis, the author acknowledges that time may modify some of his impressions and deductions.

The book is recommended as the most complete and up-to-date discussion available on penicillin therapy of syphilis.

VAMPIRE

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